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Figure 1.

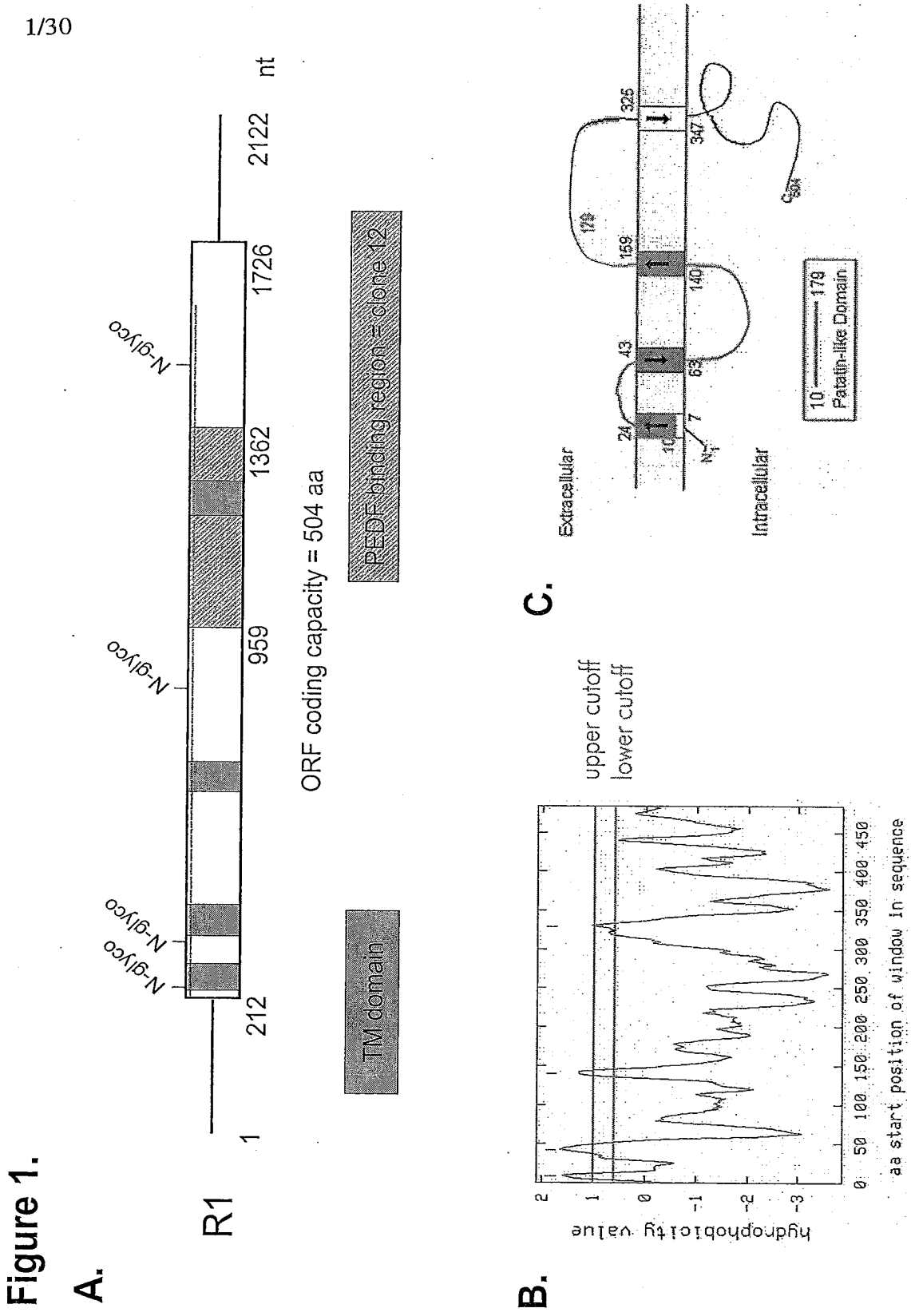
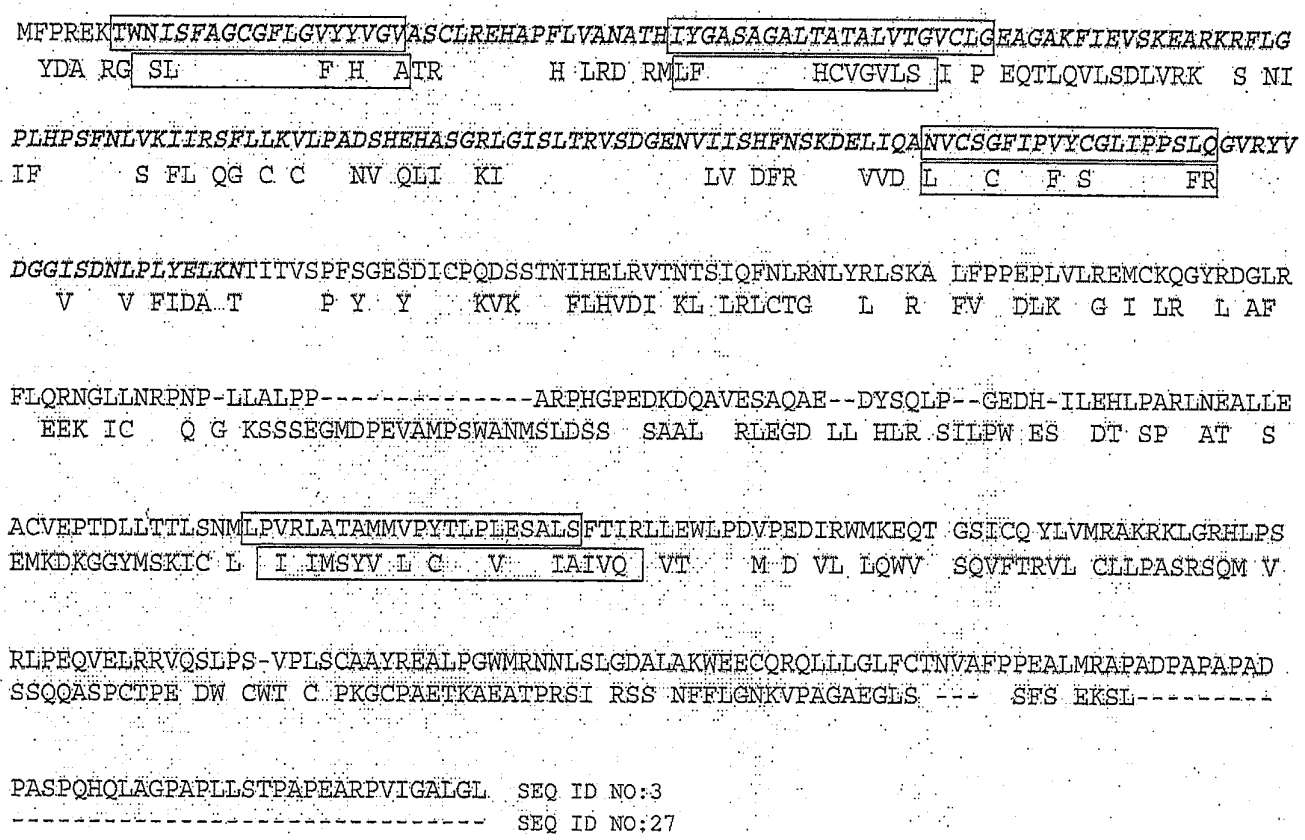

A.
R1
1
212
959
1362
1726
2122
nt
N-glyco
N-glyco
N-glyco
N-glyco
ORF coding capacity = 504 aa
PEDF binding region = clone 12
TM domain
B.
upper cutoff
lower cutoff
hydrophobicity value
2
1
0
-1
-2
-3
0 50 100 150 200 250 300 350 400 450
aa start position of window in sequence
C.
Extracellular
Intracellular
325
347
179
159
140
43
63
24
10
7
10
179
Patatin-like Domain

Figure 1.

D.



E.

253 GLLNRPN PLLALPPARP HGEPDKDQAV ESAQAEDYSQ LPGE 293 (SEQ ID NO:28)

450 T NVAFPPEALR MRAPADPAPA PADPASPQHQ LAGPAPLLST PAPEARPVIG ALGL 504 (SEQ ID NO:29)

Docket No.: NIHA-0238
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Office Action Dated: Notice to Comply Dated December 12, 2008
Replacement Sheet 2 of 30

Figure 1.

F.

Homologous patatin phospholipase A (PLA) active site in R1: **S**47 and **D**166

Active site serine

NA THIYGA**S**AGA LTA	R1	SEQ ID NO:30
YF DVIGGT**S**TGG LLT	Patatin B2	SEQ ID NO:31
CA TYVAGL**S**GST WYM	cPLA2	SEQ ID NO:32

Active site aspartic

SLQ GVRYV**D**GGIS DNLPLYE	R1	SEQ ID NO:33
ARY EFNLV**D**GAVA TVGDPAL	Patatin B2	SEQ ID NO:34
KSK KIHVV**D**SGL- TFNLPYP	cPLA2	SEQ ID NO:35

Docket No.: NIHA-0238
App No.: 10/566,540
Office Action Dated: Notice to Comply Dated December 12, 2008
Replacement Sheet 3 of 30

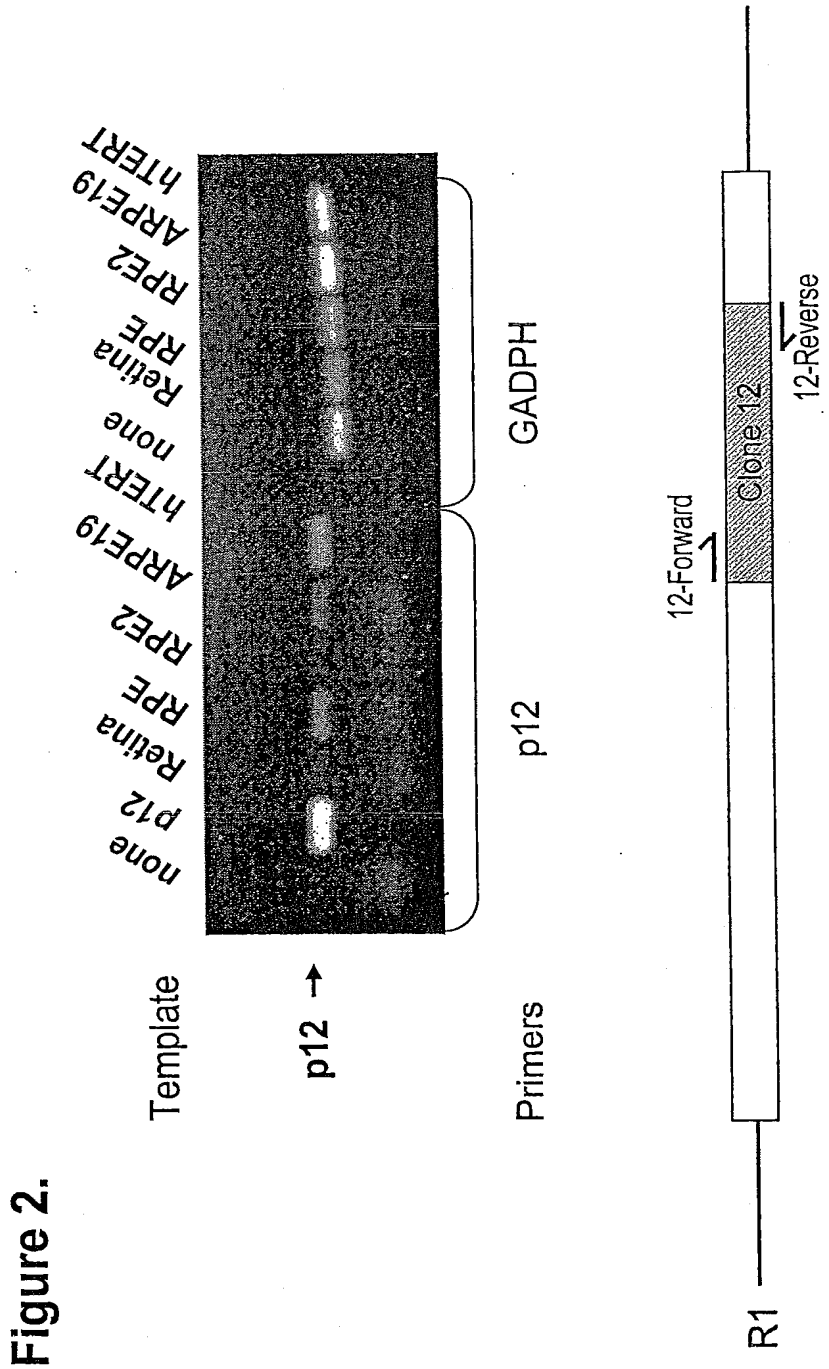

Template
p12
Primers
GADPH
p12
none
p12
Retina
RPE
RPE2
ARPE19
hTERT
none
hTERT
Retina
RPE
RPE2
ARPE19
hTERT
12-Forward
Clone 12
12-Reverse
R1

Figure 2.

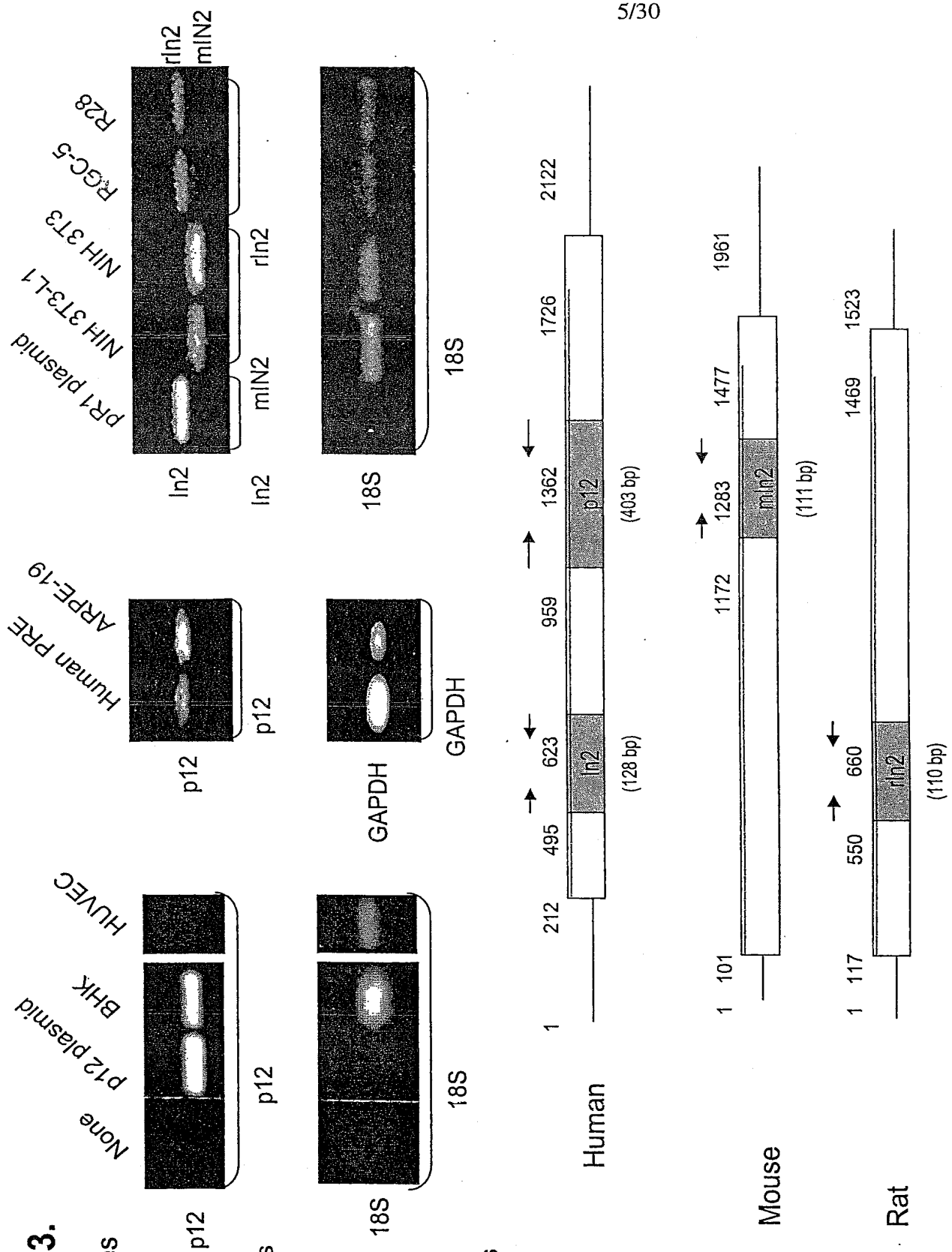
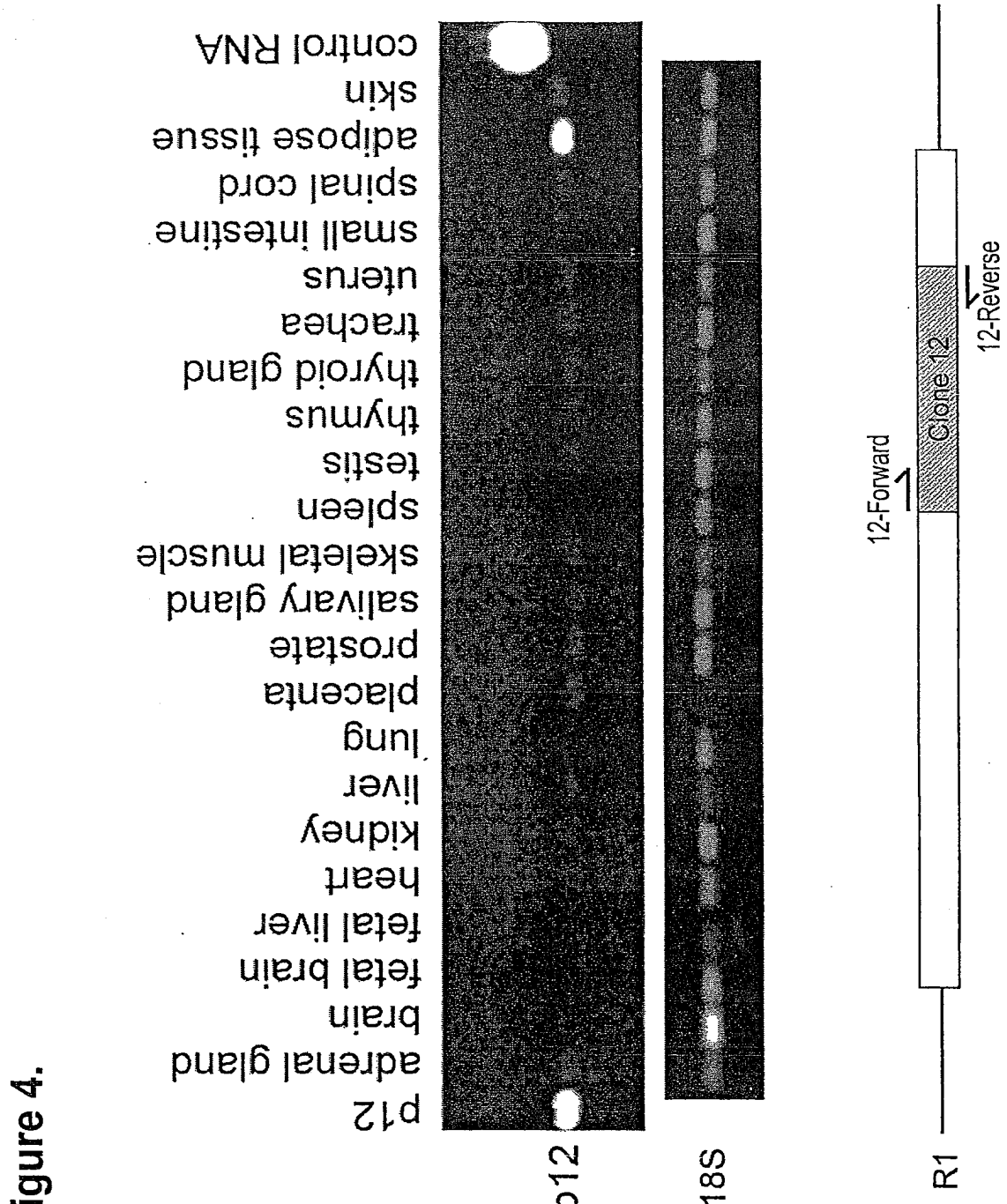


Figure 3.
Templates
None
p12 plasmid
BHK
HUVEC
p12
Primers
p12
18S
Control primers
18S
p12
Human PRE
ARPE-19
p12
GAPDH
GAPDH
rIn2
mIN2
R28
RGC-5
NIH 3T3
NIH 3T3-L1
PR1 plasmid
In2
mIN2
rIn2
In2
18S
18S
1
212
495
623
959
1362
1726
2122
In2
p12
(128 bp)
(403 bp)
Human
1
101
1172
1283
1477
1961
mIn2
(111 bp)
Mouse
1
117
550
660
1469
1523
rIn2
(110 bp)
Rat

Figure 4.


p12
adrenal gland
brain
fetal brain
fetal liver
heart
kidney
liver
lung
placenta
prostate
salivary gland
skeletal muscle
spleen
testis
thymus
thyroid gland
trachea
uterus
small intestine
spinal cord
adipose tissue
skin
control RNA
p12
18S
12-Forward
Clone 12
12-Reverse
R1

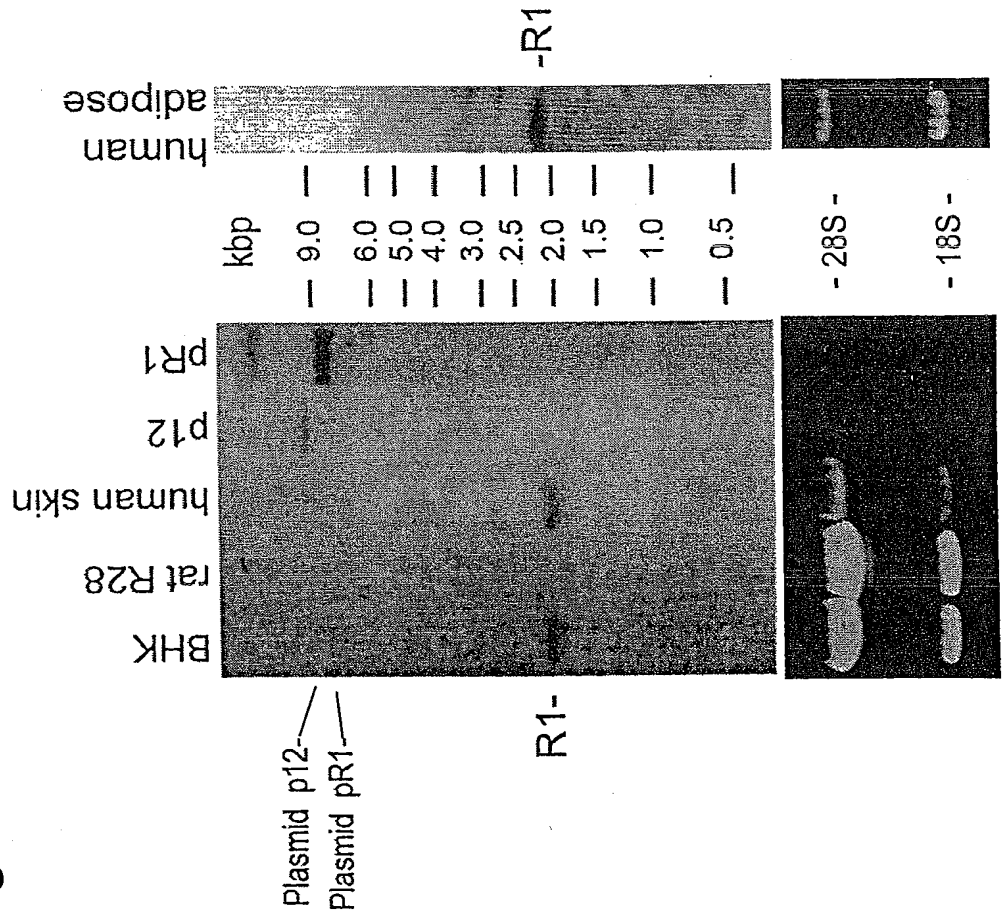
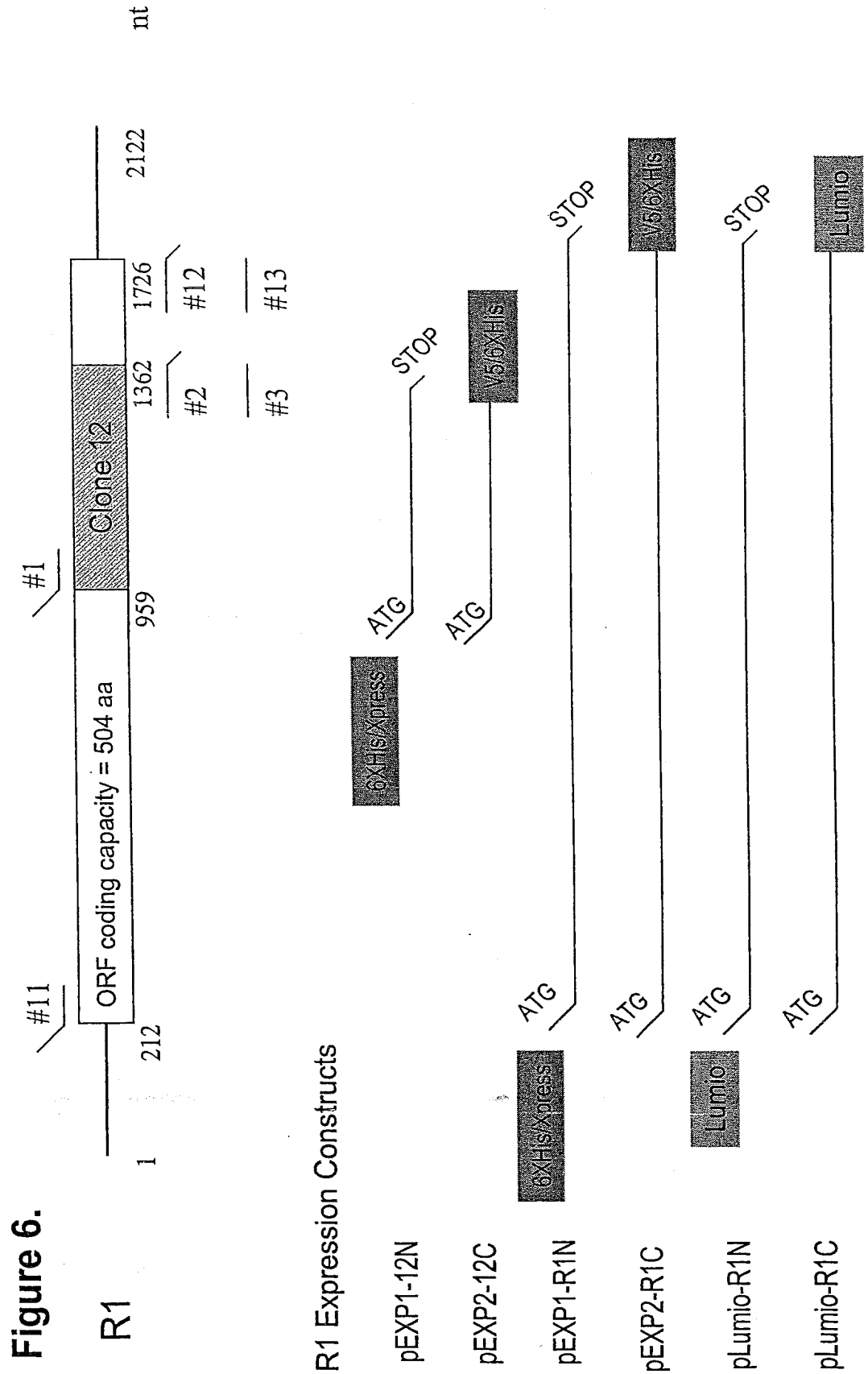

-R1
human adipose
kbp
9.0
6.0
5.0
4.0
3.0
2.5
2.0
1.5
1.0
0.5
- 28S -
- 18S -
BHK
rat R28
human skin
p12
pR1
Plasmid p12
Plasmid pR1
R1-

Figure 5.

Figure 6.


R1
nt
#11
#1
ORF coding capacity = 504 aa
Clone 12
1
212
959
1362
1726
2122
#2
#12
#3
#13
R1 Expression Constructs
pEXP1-12N
pEXP2-12C
pEXP1-R1N
pEXP2-R1C
pLumio-R1N
pLumio-R1C
ATG
STOP
6XHis/Xpress
V5/6XHis
Lumio

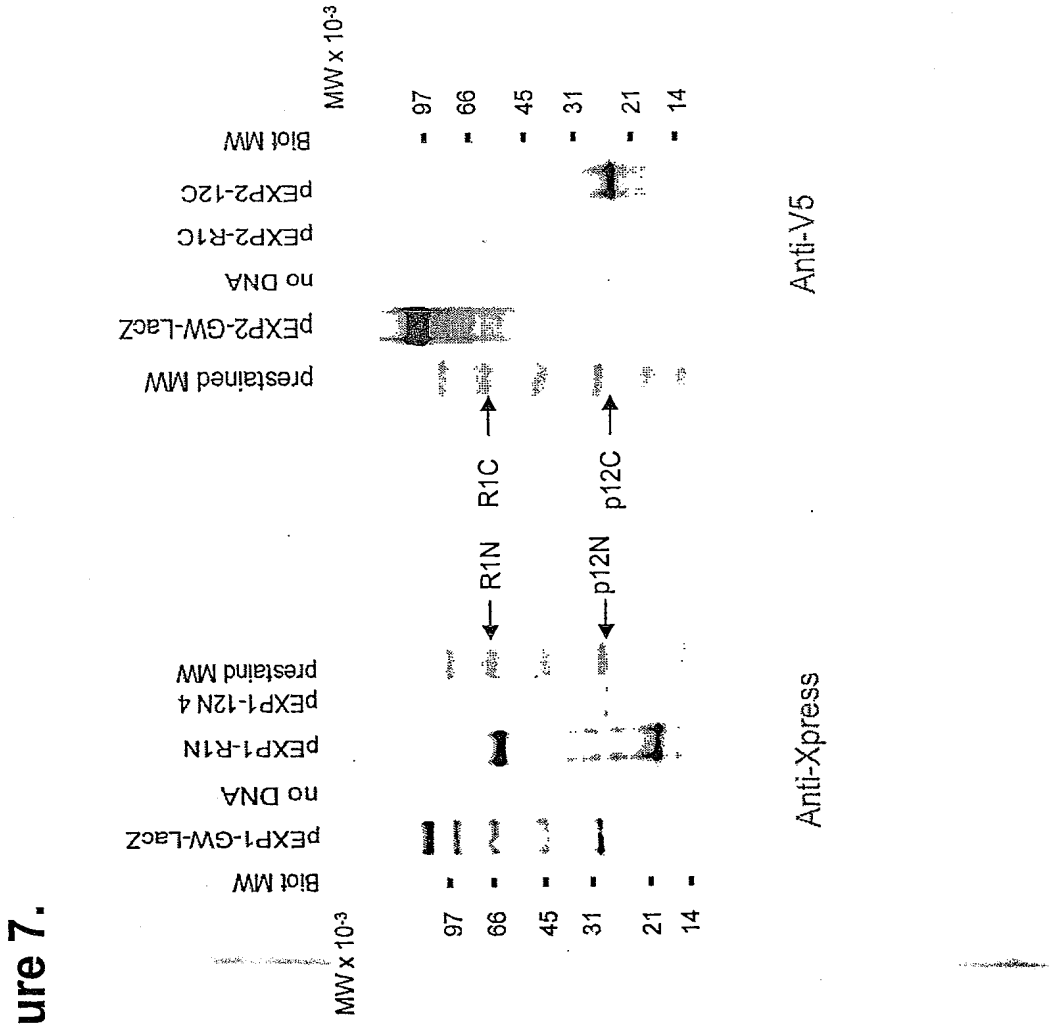
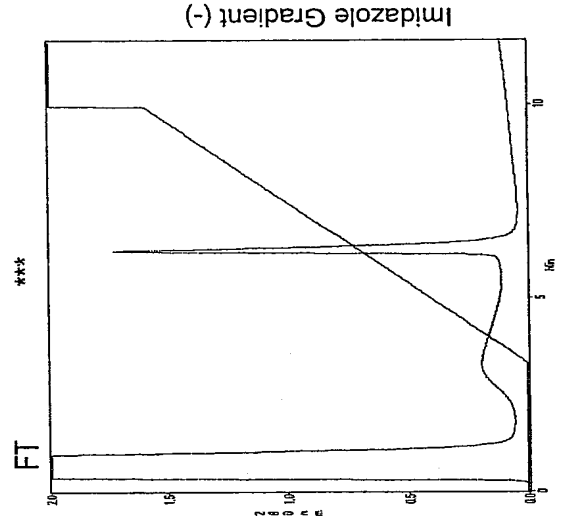

MW x 10-3
97
66
45
31
21
14
Biot MW
pEXP1-GW-LacZ
no DNA
pEXP1-R1N
pEXP1-12N 4
prestaind MW
R1N
p12N
Anti-Xpress
MW x 10-3
97
66
45
31
21
14
Biot MW
prestained MW
pEXP2-GW-LacZ
no DNA
pEXP2-R1C
pEXP2-12C
R1C
p12C
Anti-V5

Figure 7.

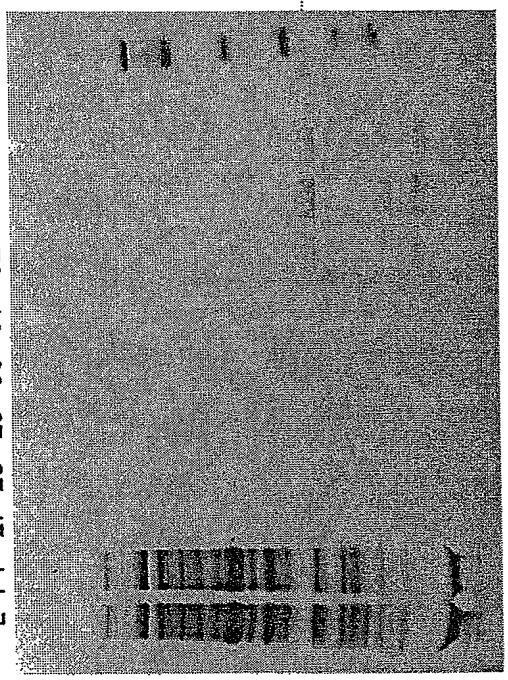
Figure 8.

A. p12

Chromatogram



SDS-PAGE
(Magic Blue stained gel)



Western (Ab-His)

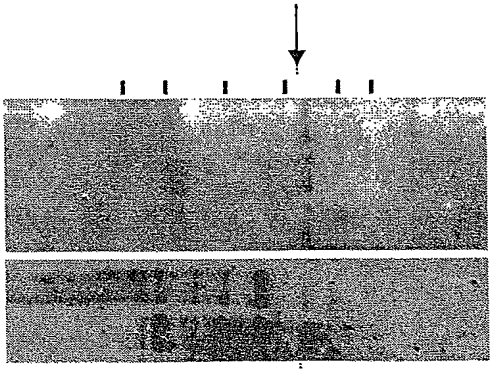
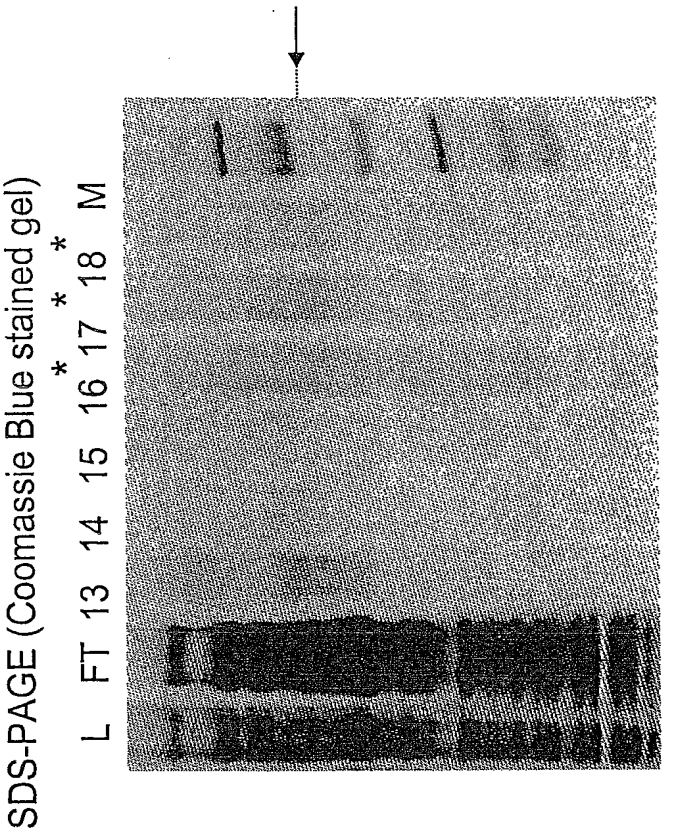


Figure 8.

B. R1


SDS-PAGE (Coomassie Blue stained gel)
L FT 13 14 15 16 17 18 M
* * *
Chromatogram
FT
***
Imidazole Gradient (-)

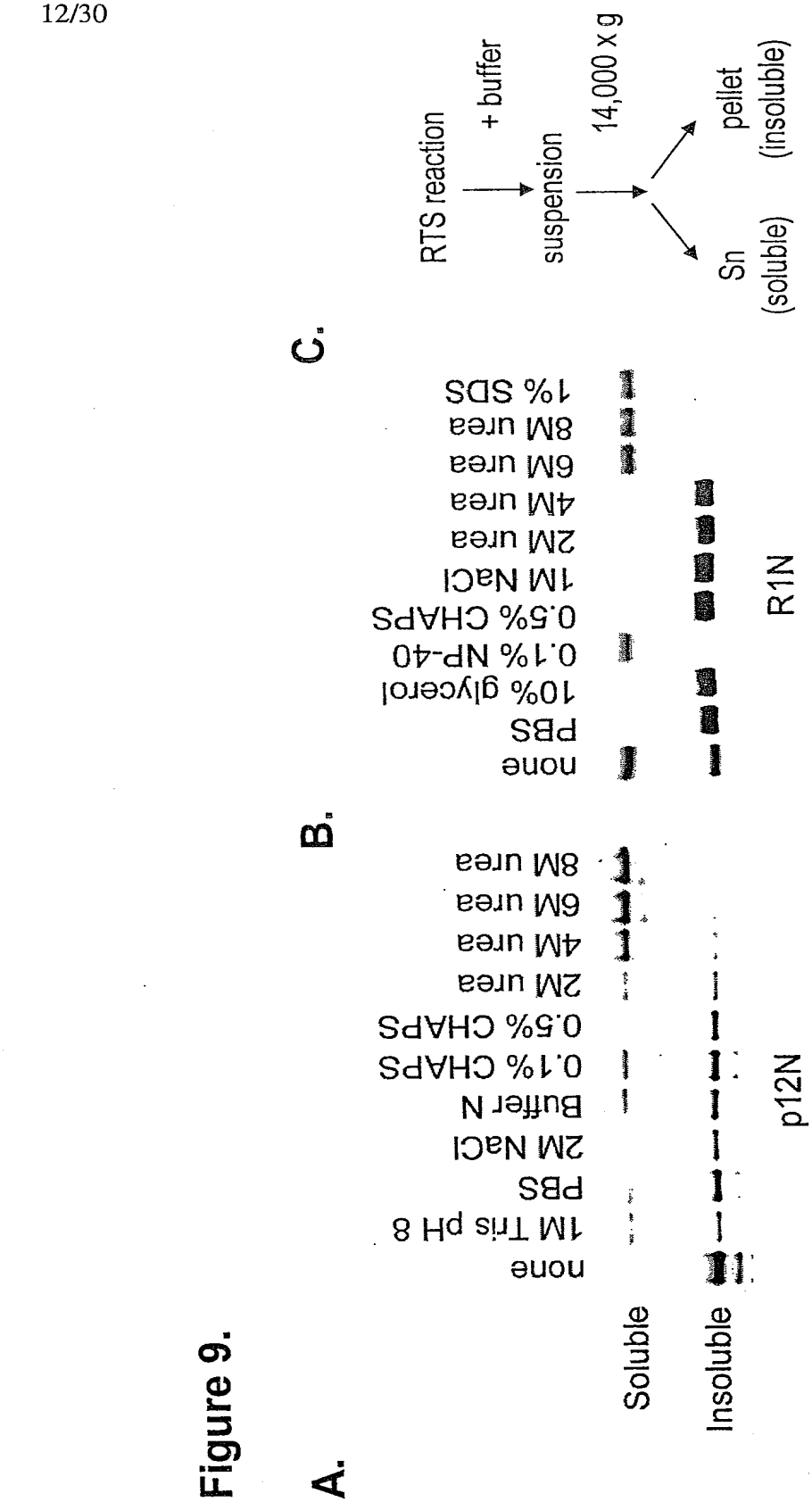

A.
Soluble
Insoluble
p12N
none
1M Tris pH 8
PBS
2M NaCl
Buffer N
0.1% CHAPS
0.5% CHAPS
2M urea
4M urea
6M urea
8M urea
B.
R1N
none
PBS
10% glycerol
0.1% NP-40
0.5% CHAPS
1M NaCl
2M urea
4M urea
6M urea
8M urea
1% SDS
C.
RTS reaction
+ buffer
suspension
14,000 x g
pellet
(insoluble)
Sn
(soluble)

Figure 9.

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Figure 10.

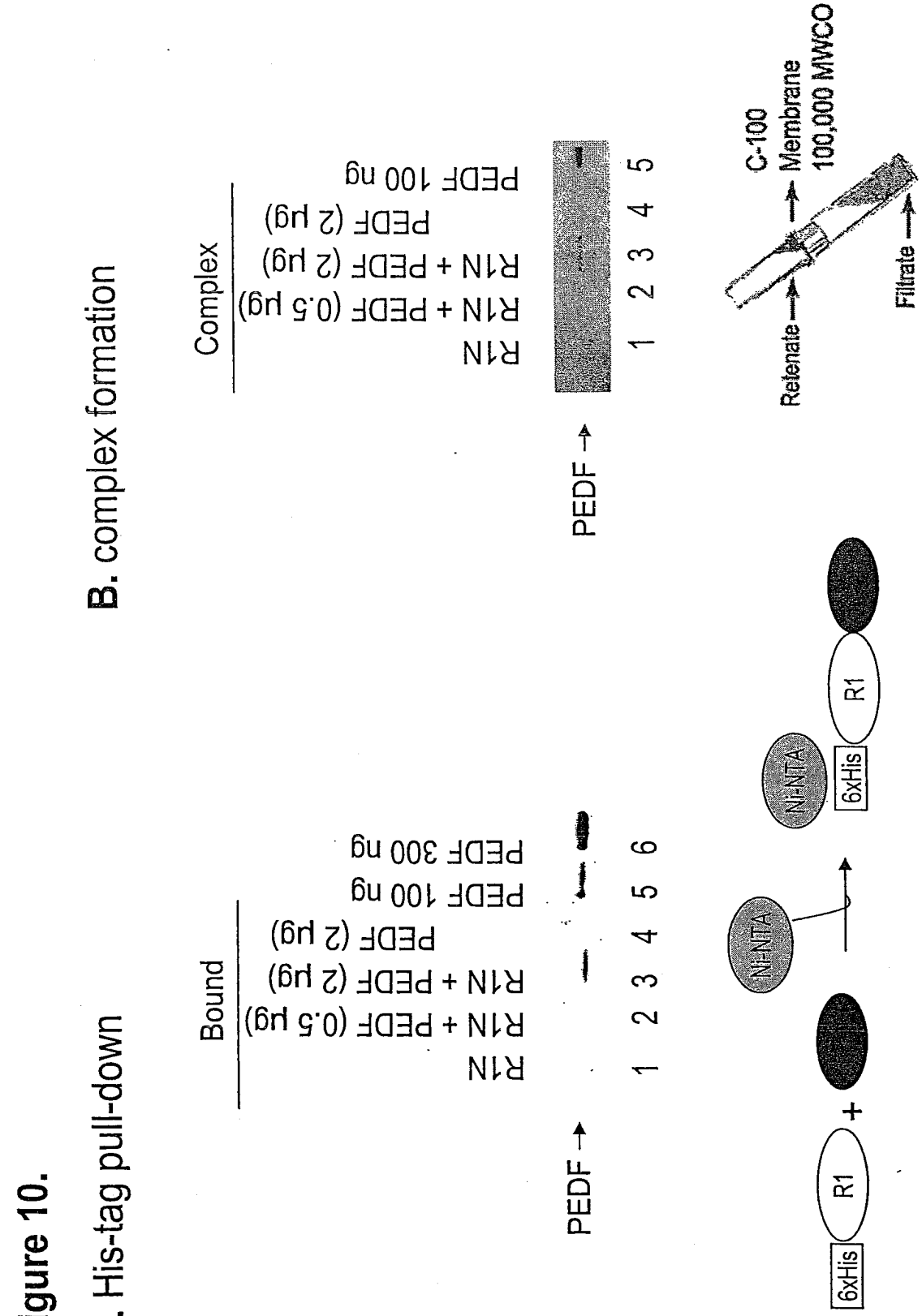

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Figure 11.

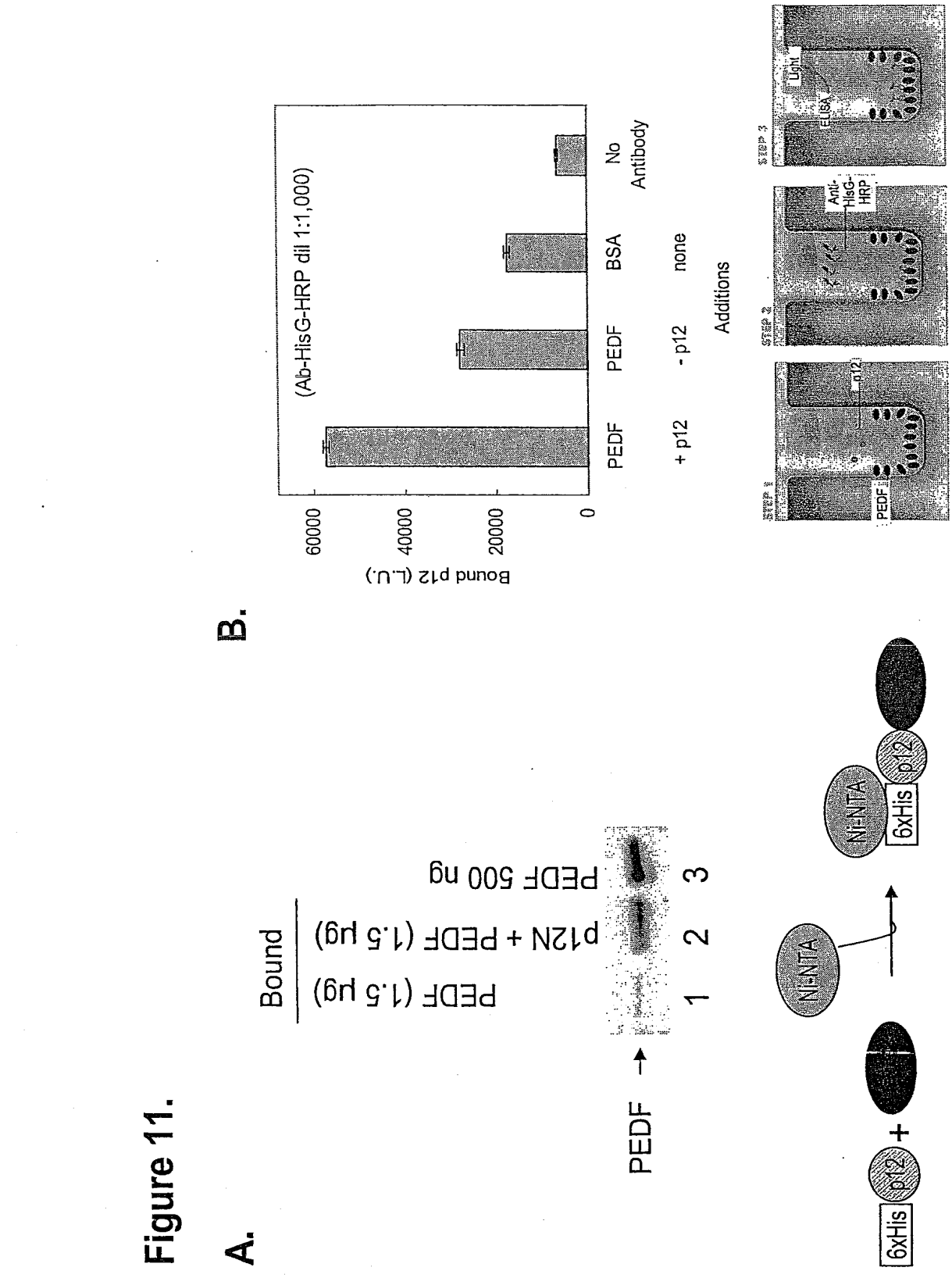


Figure 12.

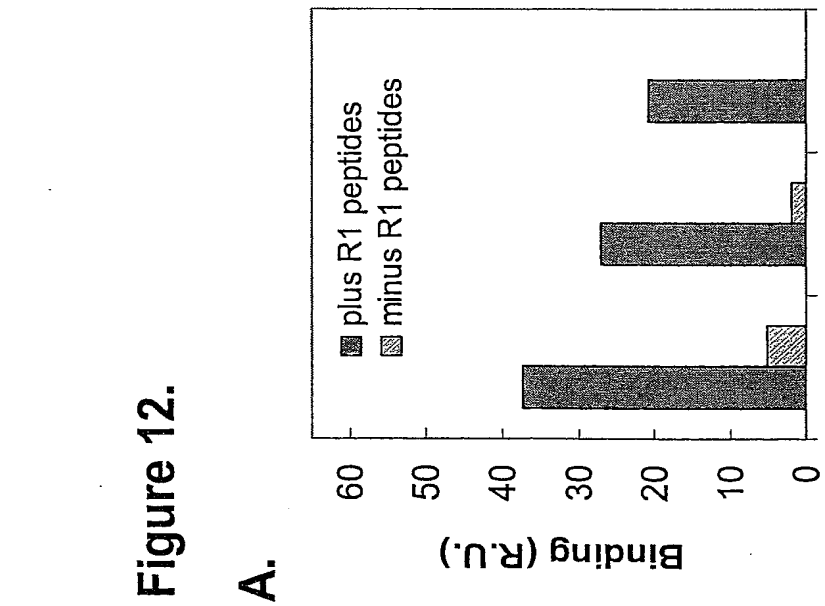

A.
Binding (R.U.)
plus R1 peptides
minus R1 peptides
IVS rxn p12N
purified p12N
IVS rxn R1N
Analytes
B.
RU
Binding (R.U.)
Time (seconds)
C.
ka (1/Ms)
kd (1/s)
KA (1/M)
KD (M)
4.41x10³
1.02 x 10⁻⁵
4.32 x 10⁸
2.31 x 10⁻⁹

Figure 13.

A.

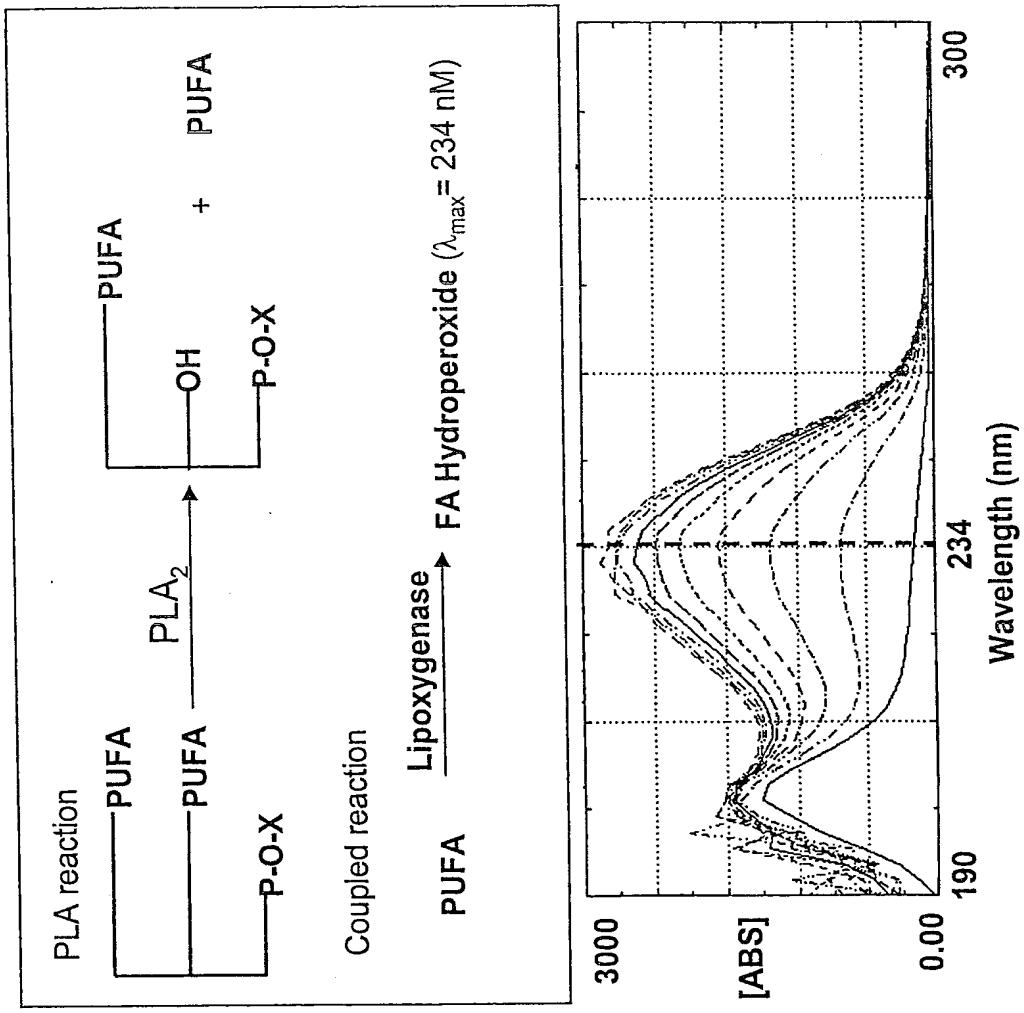
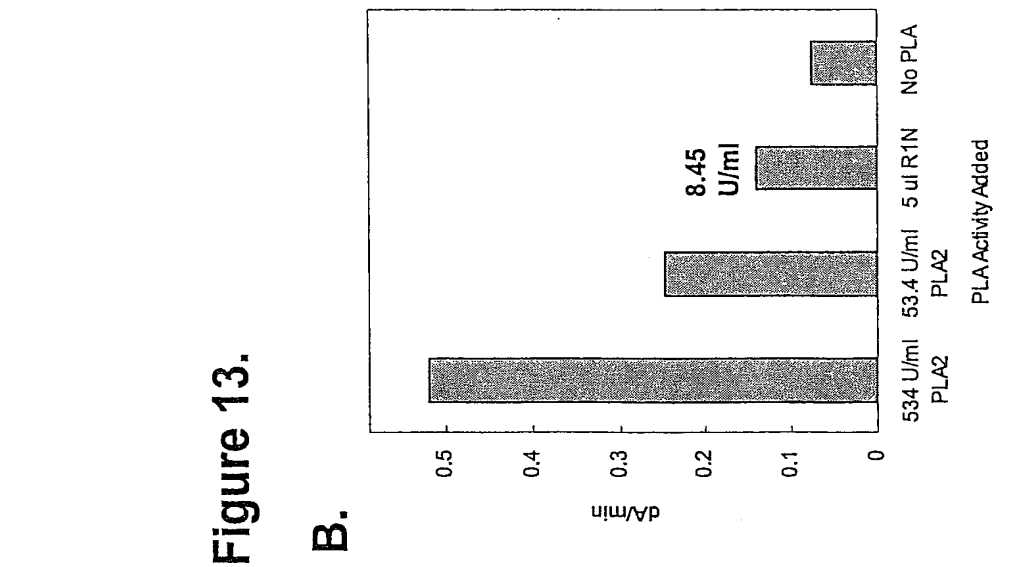
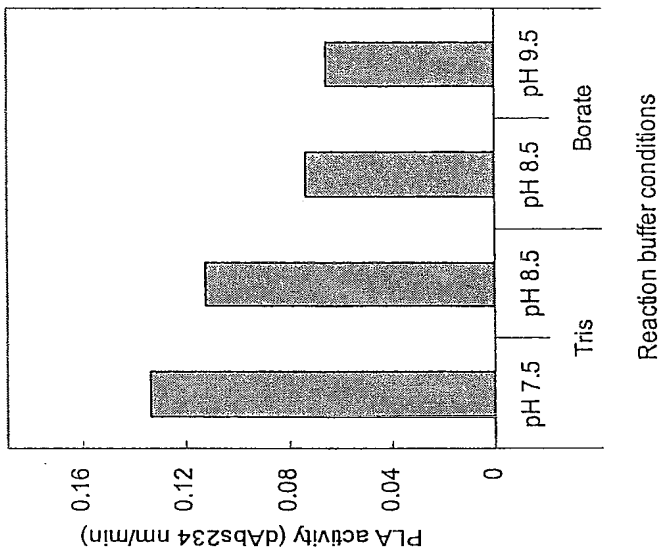

PLA reaction
PUFA
PUFA
P-O-X
PLA2
PUFA
OH
P-O-X
+
PUFA
Coupled reaction
PUFA
Lipoxygenase
FA Hydroperoxide (λmax= 234 nM)
3000
0.00
[ABS]
190
234
300
Wavelength (nm)

Figure 13.


B.
dA/min
0.5
0.4
0.3
0.2
0.1
0
8.45 U/ml
534 U/ml PLA2
53.4 U/ml PLA2
5 ul R1N
No PLA
PLA Activity Added


C.
PLA activity (dAbs234 nm/min)
0.16
0.12
0.08
0.04
0
pH 7.5
pH 8.5
Tris
pH 8.5
pH 9.5
Borate
Reaction buffer conditions

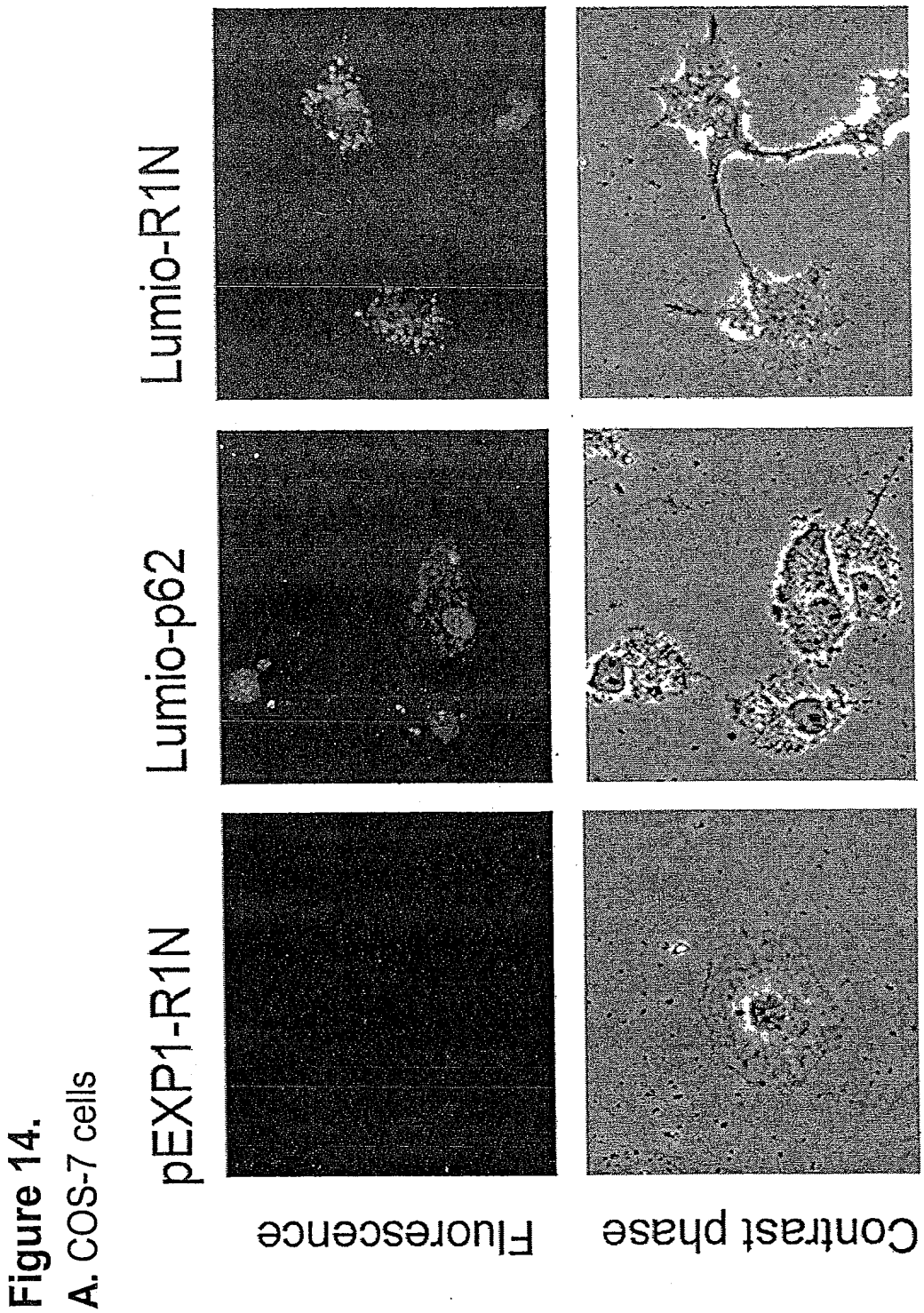


Figure 14.
A. COS-7 cells

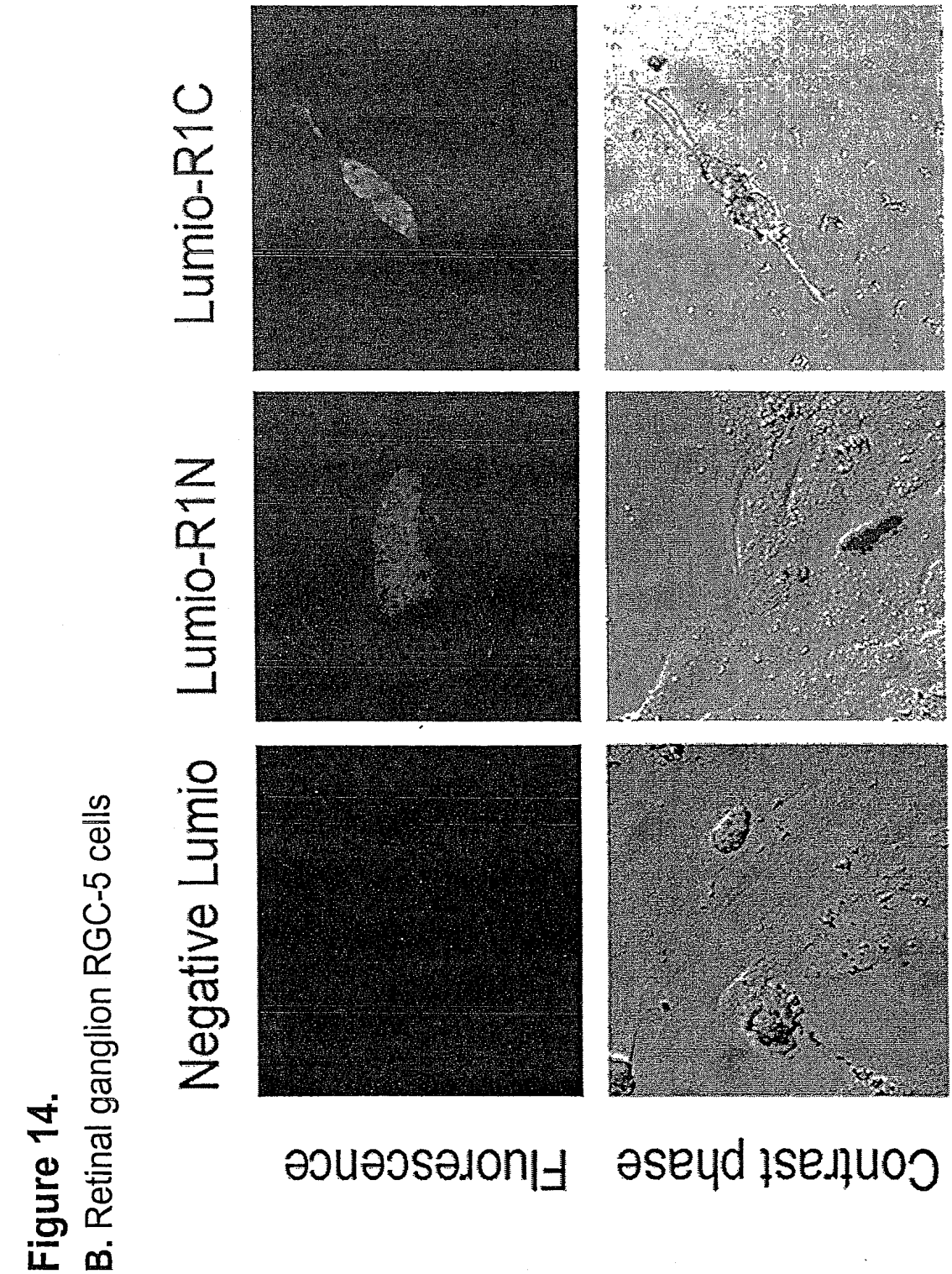
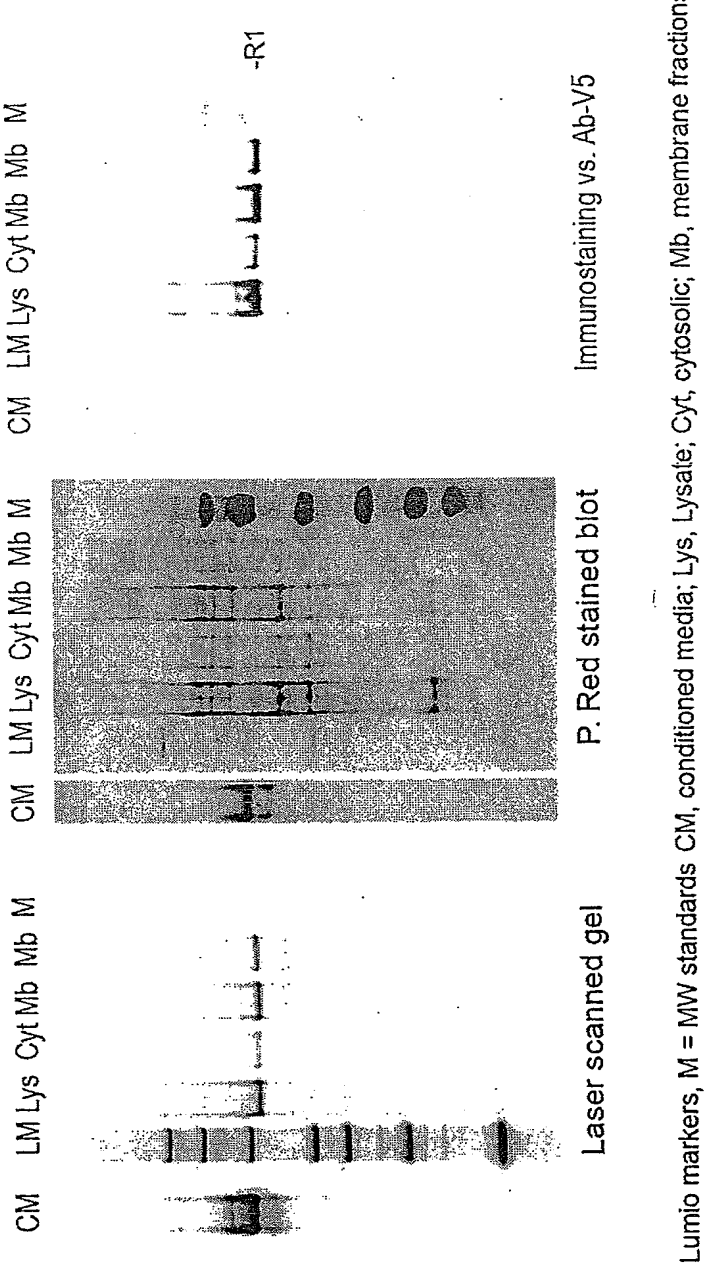
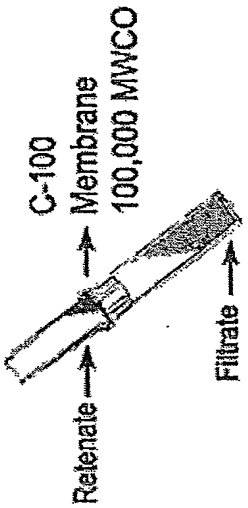


Figure 14.
B. Retinal ganglion RGC-5 cells

Figure 15.



LM= Lumio markers, M = MW standards CM, conditioned media; Lys, Lysate; Cyt, cytosolic; Mb, membrane fractions


C-100
Membrane
100,000 MWCO
Retenate
Filtrate

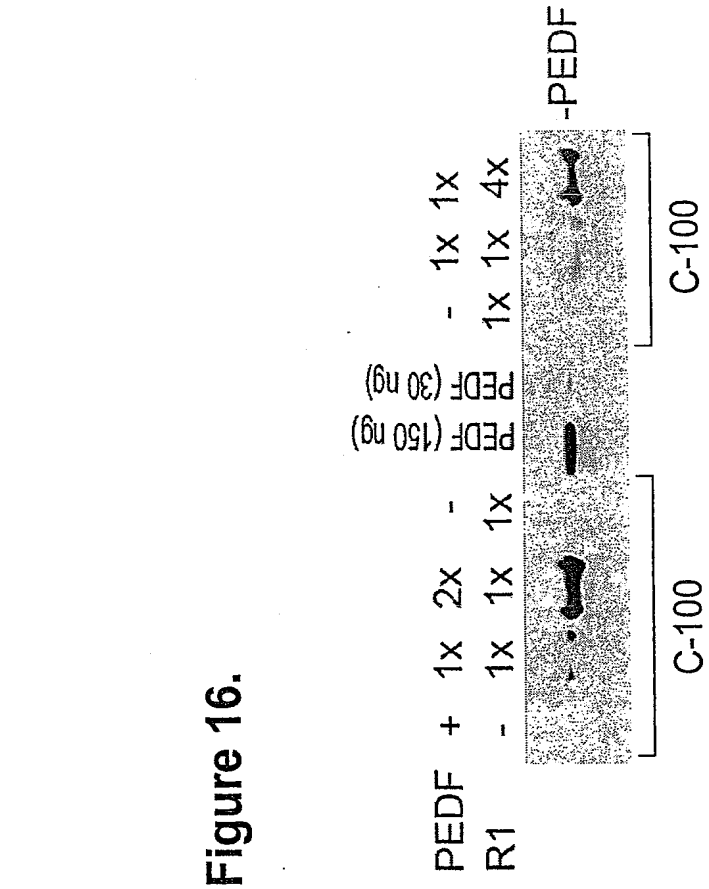
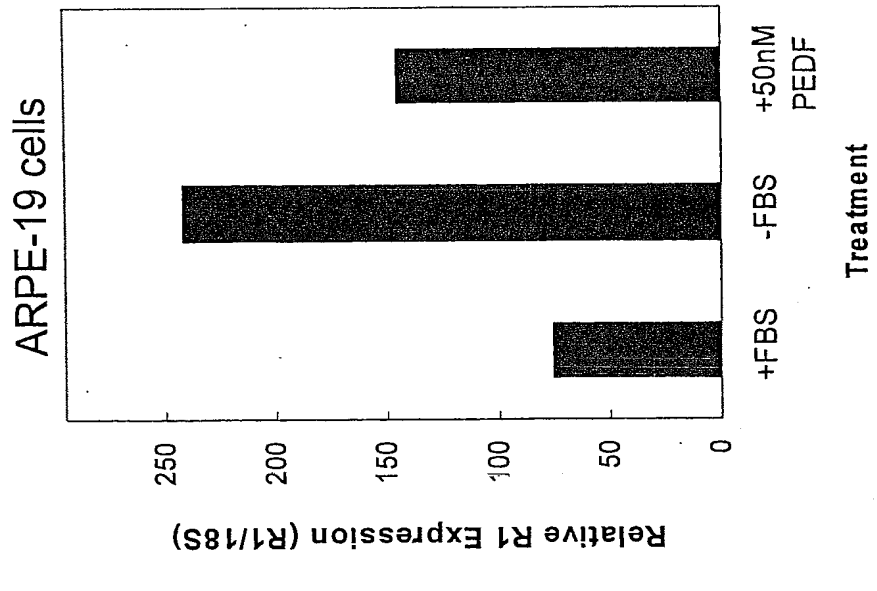
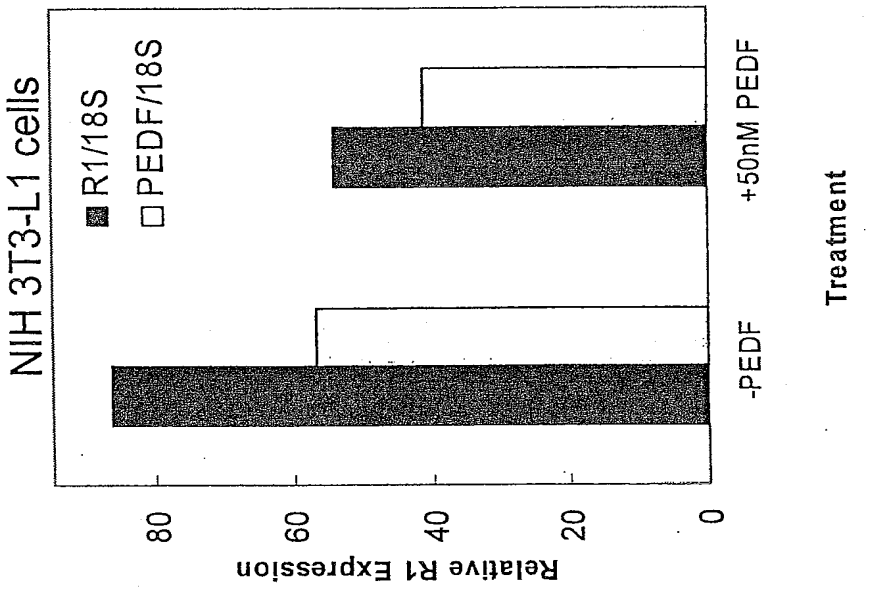

PEDF + 1x 2x - 1x 1x 4x
R1 - 1x 1x 1x 1x 1x
PEDF (150 ng)
PEDF (30 ng)
-PEDF
C-100
C-100

Figure 16.

Figure 17.

A.


ARPE-19 cells
Relative R1 Expression (R1/18S)
0
50
100
150
200
250
+FBS
-FBS
+50nM PEDF
Treatment


NIH 3T3-L1 cells
R1/18S
PEDF/18S
Relative R1 Expression
0
20
40
60
80
-PEDF
+50nM PEDF
Treatment

B.

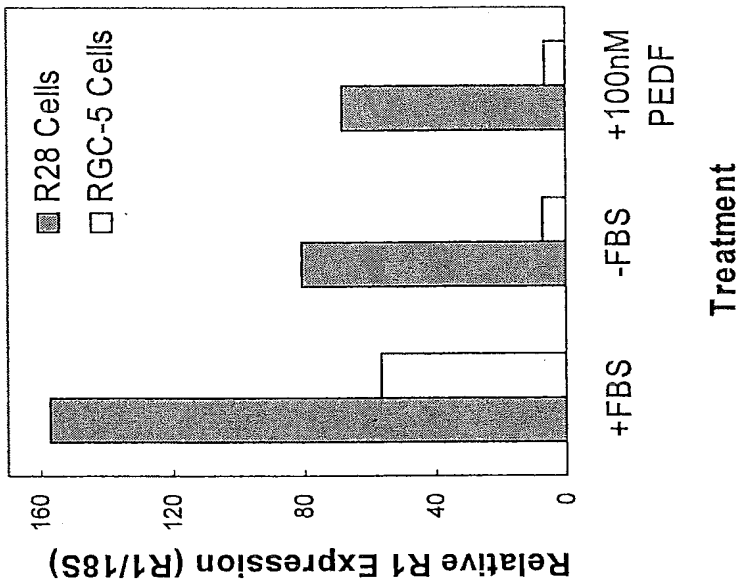

R28 Cells
RGC-5 Cells
Relative R1 Expression (R1/18S)
160
120
80
40
0
+FBS
-FBS
+100nM PEDF
Treatment

Figure 17.

Figure 17.

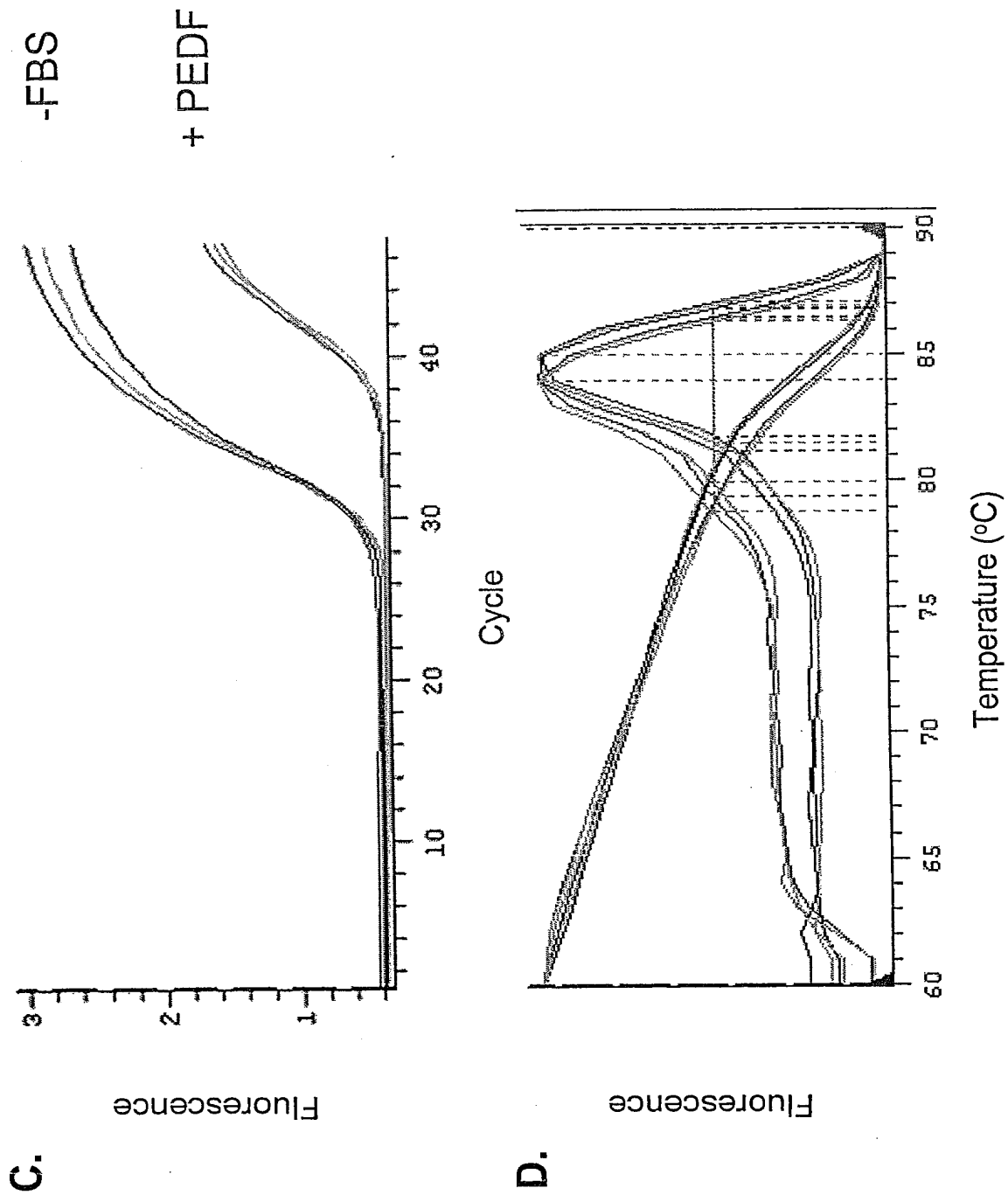

C.
-FBS
+ PEDF
Fluorescence
3
2
1
10
20
30
40
D.
Fluorescence
Cycle
Temperature (°C)
60
65
70
75
80
85
90

Figure 18.

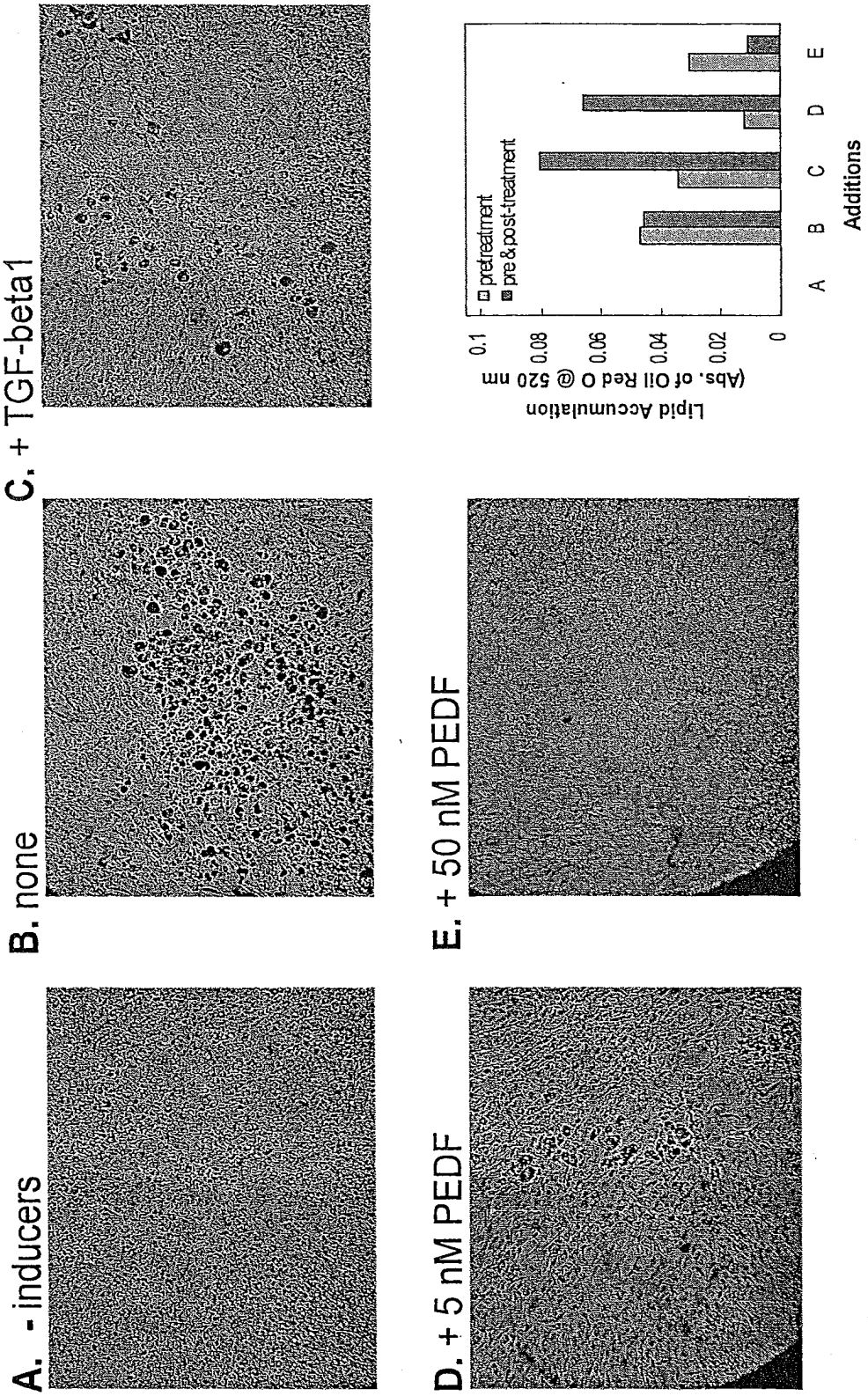

A. - inducers
B. none
C. + TGF-beta1
D. + 5 nM PEDF
E. + 50 nM PEDF
Lipid Accumulation
(Abs. of Oil Red O @ 520 nm
0.1
0.08
0.06
0.04
0.02
0
pretreatment
pre & post-treatment
A B C D E
Additions

Figure 19.

CLUSTAL W (1.82) multiple sequence alignment

```
gi|26327465|dbj|BAC27476.1|     MFPRETKWNISFAGCGFLGVYHIGVASCLREHAPFLVANATHIYGASAGA 50
gi|34861242|ref|XP_341961.1|    MFPRETKWNISFAGCGFLGVYHIGVASCLREHAPFLVANATHIYGASAGA 50
gi|16878147|gb|AAH17280.1|      MFPREKTWNISFAGCGFLGVYYVGVASCLREHAPFLVANATHIYGASAGA 50
                                ******.**************::**************************** 

gi|26327465|dbj|BAC27476.1|     LTATALVTGACLGEAGANIIEVSKEARKRFLGPLHPSFNLVKTIRGCLLK 100
gi|34861242|ref|XP_341961.1|    LTATALVTGACLGEAGANIIEVSKEARKRFLGPLHPSFNLVKTIRGCLLK 100
gi|16878147|gb|AAH17280.1|      LTATALVTGVCLGEAGAKFIEVSKEARKRFLGPLHPSFNLVKIIRSFLLK 100
                                *********.*******::********************** **. *** 

gi|26327465|dbj|BAC27476.1|     TLPADCHERANGRLGISLTRVSDGENVIISHFSSKDELIQANVCSTFIPV 150
gi|34861242|ref|XP_341961.1|    TLPADCHTRASGRLGISLTRVSDGENVIISHFSSKDELIQANVCSTFIPV 150
gi|16878147|gb|AAH17280.1|      VLPADSHEHASGRLGISLTRVSDGENVIISHFNSKDELIQANVCSGFIPV 150
                                .****.* :*.*********************.************ **** 

gi|26327465|dbj|BAC27476.1|     YCGLIPPTLQGVRYVDGGISDNLPLYELKNTITVSPFSGESDICPQDSST 200
gi|34861242|ref|XP_341961.1|    YCGLIPPTLQGVRYVDGGISDNLPLYELKNTITVSPFSGESDICPQDSST 200
gi|16878147|gb|AAH17280.1|      YCGLIPPSLQGVRYVDGGISDNLPLYELKNTITVSPFSGESDICPQDSST 200
                                *******:****************************************** 

gi|26327465|dbj|BAC27476.1|     NIHELRVTNTSIQFNLRNLYRLSKALFPPEPMVLREMCKQGYRDGLRFLR 250
gi|34861242|ref|XP_341961.1|    NIHELRITNTSIQFNLRNLYRLSKALFPPEPMVLREMCKQGYRDGLRFLR 250
gi|16878147|gb|AAH17280.1|      NIHELRVTNTSIQFNLRNLYRLSKALFPPEPLVLREMCKQGYRDGLRFLQ 250
                                ******:************************:****************: 

gi|26327465|dbj|BAC27476.1|     RNGLLNQPNPLLALPPVVPQEEDAEEAAVVEERAGEEDQLQPYRKDRILE 300
gi|34861242|ref|XP_341961.1|    RNGLLNQPNPLLALPPVVPQEEDAEEAAVTEERTGGED--------RILE 292
gi|16878147|gb|AAH17280.1|      RNGLLNRPNPLLALPPARPHGPEDKDQAVESAQAEDYSQLP--GEDHILE 298
                                ******:**********. *:  : :: ** . ::   .        :*** 

gi|26327465|dbj|BAC27476.1|     HLPARLNEALLEACVEPKDLMTTLSNMLPVRLATAMMVPYTLPLESAVSF 350
gi|34861242|ref|XP_341961.1|    HLPARLNEALLEACVEPKDLMTTLSNMLPVRLATAMMVPYTLPLESAVSF 342
gi|16878147|gb|AAH17280.1|      HLPARLNEALLEACVEPTDLLTTLSNMLPVRLATAMMVPYTLPLESALSF 348
                                *****************.**:**************************:** 

gi|26327465|dbj|BAC27476.1|     TIRLLEWLPDVPEDIRWMKEQTGSICQYLVMRAKRKLGDHLPSRLSEQVE 400
gi|34861242|ref|XP_341961.1|    TIRLLEWLPDVPEDIRWMKEQTGSICQYLVMRAKRKLGDHLPSRLSEQVE 392
gi|16878147|gb|AAH17280.1|      TIRLLEWLPDVPEDIRWMKEQTGSICQYLVMRAKRKLGRHLPSRLPEQVE 398
                                ************************************ ******.**** 

gi|26327465|dbj|BAC27476.1|     LRRAQSLPSVPLSCATYSEALPNWVRNNLSLGDALAKWEECQRQLLLGLF 450
gi|34861242|ref|XP_341961.1|    LRRAQSLPSVPLSCATYSEALPNWVRNNLSLGDALAKWEECQRQLLLGLF 442
gi|16878147|gb|AAH17280.1|      LRRVQSLPSVPLSCAAYREALPGWMRNNLSLGDALAKWEECQRQLLLGLF 448
                                ***.***********:* ****.*:************************** 

gi|26327465|dbj|BAC27476.1|     CTNVAFPPDALRMRAPAS--PTAADPATPQDPPGLPPC------------ 486
gi|34861242|ref|XP_341961.1|    CTNVAFPPDALRMRAPAS--PTATDPATPQDPSGLPPC------------ 478
gi|16878147|gb|AAH17280.1|      CTNVAFPPEALRMRAPADPAPAPADPASPQHQLAGPAPLLSTPAPEARPV 498
                                ********:********.  *:.:***:**.  . *. 

gi|26327465|dbj|BAC27476.1|     ------      (SEQ ID NO:14)
gi|34861242|ref|XP_341961.1|    ------      (SEQ ID NO:17)
gi|16878147|gb|AAH17280.1|      IGALGL 504  (SEQ ID NO:3)
```

Figure 20. (1 of 4)

CLUSTAL W (1.82) multiple sequence alignment

```
gi|26327464|dbj|AK031609.1|          ----------------------------------------------------
gi|34861241|ref|XM_341960.1|         ----------------------------------------------------
gi|16878146|gb|BC017280.1|BC01       GGCACGAGGGCGGCCCCAGTCAGACGCAGGCAGCCCCAAAGCCTGAACAG 50

gi|26327464|dbj|AK031609.1|          ----------------------------------------------------
gi|34861241|ref|XM_341960.1|         ----------------------------------------------------
gi|16878146|gb|BC017280.1|BC01       GCAGGGCCAGACCCAGCTTCTTCGCCTCCGCCAGCGGGGACCCCGAGCTA 100

gi|26327464|dbj|AK031609.1|          ----------------------------------------------------
gi|34861241|ref|XM_341960.1|         ----------------TCCTCTGCCTCCCGGCACAGCGTCTCCGCCTCCG 34
gi|16878146|gb|BC017280.1|BC01       GAGCCGCAGCGGGACCTGCCCGGCCCCCGGCTCCAGCGAGCGAGCGGCGA 150

gi|26327464|dbj|AK031609.1|          -----GGAGACCCCAAGGTATCGA-GACTGCGGGACCCACTGCCCGCAGG 44
gi|34861241|ref|XM_341960.1|         CCGGCGGGGACCCCAGGTTATCAA-GACTGCGGGACCCACTGCCCGCAGG 83
gi|16878146|gb|BC017280.1|BC01       GCAGGCGGCTCACAGAGGCCTGGCCGCCCACGGAACCCGGGGCCCGGCGG 200
                                           *   * *   *   *    * *  *** ****   *****  **

gi|26327464|dbj|AK031609.1|          ACATCGAGTCACGATGTTCCCGAGGGAGACCAAGTGGAACATCTCATTCG 94
gi|34861241|ref|XM_341960.1|         ACGTCTAATCACGATGTTCCCAAGGGAGACCAAGTGGAACATCTCGTTCG 133
gi|16878146|gb|BC017280.1|BC01       CCGCC--GCCGCGATGTTTCCCCGCGAGAAGACGTGGAACATCTCGTTCG 248
                                      *  *    * ******* **  * ****  * ************ ****

gi|26327464|dbj|AK031609.1|          CTGGCTGCGGCTTCCTCGGGGTCTACCACATTGGCGTGGCCTCCTGCCTC 144
gi|34861241|ref|XM_341960.1|         CTGGCTGCGGCTTCCTCGGGGTCTACCACATTGGAGTGGCCTCCTGCCTC 183
gi|16878146|gb|BC017280.1|BC01       CGGGCTGCGGCTTCCTCGGCGTCTACTACGTCGGCGTGGCCTCCTGCCTC 298
                                     * ***************** ****** ** * ** ***************

gi|26327464|dbj|AK031609.1|          CGTGAGCACGCGCCCTTCCTGGTGGCCAACGCCACTCACATCTACGGAGC 194
gi|34861241|ref|XM_341960.1|         CGTGAGCACGCGCCCTTCCTGGTGGCCAACGCCACTCACATCTACGGAGC 233
gi|16878146|gb|BC017280.1|BC01       CGCGAGCACGCGCCCTTCCTGGTGGCCAACGCCACGCACATCTACGGCGC 348
                                     ** ******************************** *********** **

gi|26327464|dbj|AK031609.1|          CTCGGCAGGGGCGCTCACCGCCACAGCGCTGGTCACTGGGGCCTGCCTGG 244
gi|34861241|ref|XM_341960.1|         CTCGGCAGGGGCGCTTACCGCCACAGCGCTGGTCACTGGGGCCTGCCTGG 283
gi|16878146|gb|BC017280.1|BC01       CTCGGCCGGGGCGCTCACGGCCACGGCGCTGGTCACCGGGGTCTGCCTGG 398
                                     ****** ******** ** ***** *********** **** ********

gi|26327464|dbj|AK031609.1|          GTGAAGCAGGTGCCAACATTATTGAGGTGTCCAAGGAGGCCCGGAAGCGG 294
gi|34861241|ref|XM_341960.1|         GCGAAGCGGGTGCCAACATTATTGAGGTGTCCAAGGAGGCTCGGAAGCGG 333
gi|16878146|gb|BC017280.1|BC01       GTGAGGCTGGTGCCAAGTTCATTGAGGTATCTAAAGAGGCCCGGAAGCGG 448
                                     * ** ** ********  * ******** ** ** ***** *********

gi|26327464|dbj|AK031609.1|          TTCCTGGGTCCTCTGCATCCCTCCTTCAACCTGGTGAAGACCATCCGTGG 344
gi|34861241|ref|XM_341960.1|         TTCCTGGGTCCCCTGCACCCCTCCTTCAACCTGGTAAAGACCATCCGTGG 383
gi|16878146|gb|BC017280.1|BC01       TTCCTGGGCCCCCTGCACCCCTCCTTCAACCTGGTAAAGATCATCCGCAG 498
                                     ******** ** ***** ***************** **** ******  *

gi|26327464|dbj|AK031609.1|          CTGTCTACTAAAGACCCTGCCTGCTGATTGCCATGAGCGCGCCAATGGAC 394
gi|34861241|ref|XM_341960.1|         TTGTCTACTGAAGACCCTGCCTGCTGATTGCCACACGCGTGCCAGCGGAC 433
gi|16878146|gb|BC017280.1|BC01       TTTCCTGCTGAAGGTCCTGCCTGCTGATAGCCATGAGCATGCCAGTGGGC 548
                                      *  ** ** ***  ************* ****   **  ****  ** *

gi|26327464|dbj|AK031609.1|          GCCTGGGCATCTCCCTGACTCGTGTTTCAGACGGAGAGAACGTCATCATA 444
gi|34861241|ref|XM_341960.1|         GCCTGGGCATCTCCCTGACTCGAGTTTCGGATGGAGAGAATGTCATCATA 483
gi|16878146|gb|BC017280.1|BC01       GCCTGGGCATCTCCCTGACCCGCGTGTCAGACGGCGAGAATGTCATTATA 598
                                     ******************* ** ** ** ** ** ***** ***** ***
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Figure 20. (2 of 4)

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gi|26327464|dbj|AK031609.1|          TCCCACTTTAGCTCCAAGGATGAGCTCATCCAGGCCAATGTCTGCAGCAC 494
gi|34861241|ref|XM_341960.1|         TCGCACTTTAGCTCCAAGGATGAGCTTATCCAGGCCAATGTTTGCAGCAC 533
gi|16878146|gb|BC017280.1|BC01       TCCCACTTCAACTCCAAGGACGAGCTCATCCAGGCCAATGTCTGCAGCGG 648
                                     ** ***** * ********* ***** ************** ******

gi|26327464|dbj|AK031609.1|          ATTTATCCCGGTGTACTGTGGCCTCATTCCTCCTACCCTCCAAGGGGTGC 544
gi|34861241|ref|XM_341960.1|         TTTTATCCCTGTGTACTGTGGCCTCATTCCTCCTACCCTTCAAGGGGTGC 583
gi|16878146|gb|BC017280.1|BC01       TTTCATCCCCGTGTACTGTGGGCTCATCCCTCCCTCCCTCCAGGGGGTGC 698
                                      ** ***** *********** ***** *****  **** ** *******

gi|26327464|dbj|AK031609.1|          GCTATGTGGATGGCGGCATTTCAGACAACTTGCCACTTTATGAGCTGAAG 594
gi|34861241|ref|XM_341960.1|         GCTATGTGGATGGCGGCATTTCAGACAACTTGCCACTTTATGAGCTGAAG 633
gi|16878146|gb|BC017280.1|BC01       GCTACGTGGATGGTGGCATTTCAGACAACCTGCCACTCTATGAGCTTAAG 748
                                     **** ******** *************** ******* ******** ***

gi|26327464|dbj|AK031609.1|          AATACCATCACAGTGTCCCCATTCTCAGGCGAGAGTGACATCTGCCCTCA 644
gi|34861241|ref|XM_341960.1|         AATACCATCACAGTGTCCCCATTCTCAGGCGAGAGTGACATCTGCCCACA 683
gi|16878146|gb|BC017280.1|BC01       AACACCATCACAGTGTCCCCCTTCTCGGGCGAGAGTGACATCTGTCCGCA 798
                                     ** ***************** ***** ***************** ** **

gi|26327464|dbj|AK031609.1|          GGACAGCTCCACCAACATCCACGAGCTTCGCGTCACCAACACCAGCATCC 694
gi|34861241|ref|XM_341960.1|         AGACAGCTCCACCAACATCCACGAACTTCGTATCACCAACACCAGCATCC 733
gi|16878146|gb|BC017280.1|BC01       GGACAGCTCCACCAACATCCACGAGCTGCGGGTCACCAACACCAGCATCC 848
                                      ********************** ** **  ******************

gi|26327464|dbj|AK031609.1|          AGTTCAACCTTCGCAATCTCTACCGCCTCTCGAAGGCTCTCTTCCCGCCA 744
gi|34861241|ref|XM_341960.1|         AATTCAACCTGCGCAATCTCTACCGCCTCTCGAAGGCTCTCTTCCCGCCA 783
gi|16878146|gb|BC017280.1|BC01       AGTTCAACCTGCGCAACCTCTACCGCCTCTCCAAGGCCCTCTTCCCGCCG 898
                                     * ******** ***** *************** ***** ***********

gi|26327464|dbj|AK031609.1|          GAGCCCATGGTCCTCCGAGAGATGTGCAAACAGGGCTACAGAGATGGACT 794
gi|34861241|ref|XM_341960.1|         GAGCCCATGGTTCTCCGAGAGATGTGCAAACAGGGCTACCGAGATGGACT 833
gi|16878146|gb|BC017280.1|BC01       GAGCCCCTGGTGCTGCGAGAGATGTGCAAGCAGGGATACCGGGATGGCCT 948
                                     ****** **** ** ************** ***** *** * ***** **

gi|26327464|dbj|AK031609.1|          TCGATTCCTTAGGAGGAATGGCCTACTGAACCAACCCAACCCTTTGCTGG 844
gi|34861241|ref|XM_341960.1|         TCGATTCCTTAGGAGGAATGGCCTACTGAACCAACCCAACCCTTTGCTGG 883
gi|16878146|gb|BC017280.1|BC01       GCGCTTTCTGCAGCGGAACGGCCTCCTGAACCGGCCCAACCCCTTGCTGG 998
                                      ** ** **   * **** ***** *******  ******** *******

gi|26327464|dbj|AK031609.1|          CACTGCCCCCAGTTGTCCCCCAGGAAGAGGATGCAGAGGAAGCTGCTGTG 894
gi|34861241|ref|XM_341960.1|         CACTGCCCCCGGTTGTCCCCCAGGAAGAGGATGCAGAGGAAGCTGCCGTG 933
gi|16878146|gb|BC017280.1|BC01       CGTTGCCCCCCGCCCGCCCCCACGG------CCCAGAGGACAAGGACCAG 1042
                                     *  ******* *    ****** *         *******    *    *

gi|26327464|dbj|AK031609.1|          GTGGAGGAGAGGGCTGGAGAGGAGGATCAATTGCAGCCTTATAGAAAAGA 944
gi|34861241|ref|XM_341960.1|         ACTGAGGAGAGGACTGGAGGGGAGGATC---------------------- 961
gi|16878146|gb|BC017280.1|BC01       GCAGTGGAGAGCGCCCAAGCGGAGGATTACTCGCAGCTGCCGGGAGAAGA 1092
                                        * ******  *   ** *******

gi|26327464|dbj|AK031609.1|          TCGAATTCTAGAGCACCTGCCTGCCAGACTCAATGAGGCCCTGCTGGAGG 994
gi|34861241|ref|XM_341960.1|         --GGATTCTAGAGCACCTGCCTGCCAGACTCAACGAGGCCCTGCTGGAGG 1009
gi|16878146|gb|BC017280.1|BC01       TCACATCCTGGAGCACCTGCCCGCCCGGCTCAATGAGGCCCTGCTGGAGG 1142
                                         ** ** ************ *** * ***** ****************

gi|26327464|dbj|AK031609.1|          CCTGTGTGGAACCAAAGGACCTGATGACCACCCTTTCCAACATGCTACCA 1044
gi|34861241|ref|XM_341960.1|         CCTGTGTGGAACCGAAAGACCTGATGACCACCCTTTCCAACATGCTGCCA 1059
gi|16878146|gb|BC017280.1|BC01       CCTGCGTGGAGCCCACGGACCTGCTGACCACCCTCTCCAACATGCTGCCT 1192
                                     **** ***** ** *  ****** ********** *********** **
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Figure 20. (3 of 4)

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gi|26327464|dbj|AK031609.1|          GTGCGCCTGGCAACGGCCATGATGGTGCCCTATACTCTGCCGCTGGAGAG 1094
gi|34861241|ref|XM_341960.1|         GTGCGCCTGGCCACTGCCATGATGGTACCCTATACTCTGCCACTGGAGAG 1109
gi|16878146|gb|BC017280.1|BC01       GTGCGTCTGGCCACGGCCATGATGGTGCCCTACACGCTGCCGCTGGAGAG 1242
                                     ***** ***** ** *********** ***** ** ***** ********

gi|26327464|dbj|AK031609.1|          TGCAGTGTCCTTCACCATCCGCTTGTTGGAGTGGCTGCCTGATGTCCCTG 1144
gi|34861241|ref|XM_341960.1|         CGCAGTGTCCTTCACCATCCGTTTGTTGGAGTGGCTGCCTGATGTCCCTG 1159
gi|16878146|gb|BC017280.1|BC01       CGCTCTGTCCTTCACCATCCGCTTGCTGGAGTGGCTGCCCGACGTTCCCG 1292
                                      **  ********************* *** ************* ** ** ** *

gi|26327464|dbj|AK031609.1|          AAGATATCCGGTGGATGAAAGAGCAGACGGGTAGCATCTGCCAGTATCTG 1194
gi|34861241|ref|XM_341960.1|         AGGATATCCGGTGGATGAAGGAGCAGACAGGTAGCATCTGCCAGTATCTG 1209
gi|16878146|gb|BC017280.1|BC01       AGGACATCCGGTGGATGAAGGAGCAGACGGGCAGCATCTGCCAGTACCTG 1342
                                     * ** ********************* ******** ** ********************

gi|26327464|dbj|AK031609.1|          GTGATGAGGGCCAAGAGGAAATTGGGTGACCATCTGCCTTCCAGACTGTC 1244
gi|34861241|ref|XM_341960.1|         GTGATGAGGGCCAAGAGGAAATTGGGTGACCATCTACCTTCCAGACTGTC 1259
gi|16878146|gb|BC017280.1|BC01       GTGATGCGCGCCAAGAGGAAGCTGGGCAGGCACCTGCCCTCCAGGCTGCC 1392
                                     ****** * ***********  ****    ** ** ** ***** *** * *

gi|26327464|dbj|AK031609.1|          TGAGCAGGTGGAACTGCGACGTGCCCAGTCTCTGCCCTCTGTGCCACTGT 1294
gi|34861241|ref|XM_341960.1|         TGAGCAGGTGGAGCTGCGGCGTGCCCAGTCTCTGCCGTCTGTGCCACTGT 1309
gi|16878146|gb|BC017280.1|BC01       GGAGCAGGTGGAGCTGCGCCGCGTCCAGTCGCTGCCGTCCGTGCCGCTGT 1442
                                      *********** ***** ** * ****** ***** ** ***** ****

gi|26327464|dbj|AK031609.1|          CTTGCGCCACCTACAGTGAGGCCCTACCCAACTGGGTACGAAACAACCTC 1344
gi|34861241|ref|XM_341960.1|         CTTGCGCCACCTACAGTGAGGCACTGCCCAACTGGGTACGAAACAACCTC 1359
gi|16878146|gb|BC017280.1|BC01       CCTGCGCCGCCTACAGAGAGGCACTGCCCGGCTGGATGCGCAACAACCTC 1492
                                     * ****** ******* ***** ** ***  **** * ** *********

gi|26327464|dbj|AK031609.1|          TCACTGGGGGACGCGCTGGCCAAGTGGGAAGAATGCCAGCGTCAGCTACT 1394
gi|34861241|ref|XM_341960.1|         TCACTGGGGGACGCGCTGGCCAAGTGGGAAGAATGCCAGCGTCAGCTACT 1409
gi|16878146|gb|BC017280.1|BC01       TCGCTGGGGGACGCGCTGGCCAAGTGGGAGGAGTGCCAGCGCCAGCTGCT 1542
                                     ** ************************** ** ******** ***** **

gi|26327464|dbj|AK031609.1|          GCTGGGTCTCTTCTGCACCAATGTGGCCTTCCCGCCGGATGCCTTGCGCA 1444
gi|34861241|ref|XM_341960.1|         GCTGGGTCTCTTCTGCACCAATGTGGCCTTCCCGCCTGATGCCTTGCGCA 1459
gi|16878146|gb|BC017280.1|BC01       GCTCGGCCTCTTCTGCACCAACGTGGCCTTCCCGCCCGAAGCTCTGCGCA 1592
                                     *** ** ************** ************** ** **  ******

gi|26327464|dbj|AK031609.1|          TGCGCGCACCTGCCAGCCC------CACTGCCGCAGATCCTGCCACCCCA 1488
gi|34861241|ref|XM_341960.1|         TGCGCGCACCTGCCAGCCC------CACCGCCACAGATCCTGCCACCCCA 1503
gi|16878146|gb|BC017280.1|BC01       TGCGCGCACCCGCCGACCCGGCTCCCGCCCCCGCGGACCCAGCATCCCCG 1642
                                     ********** ***  ***      * *  ** * ** ** **  ****

gi|26327464|dbj|AK031609.1|          CAGGATCCAC----CTGGCCTCCCGCCTTGCTGAGAATCACCATTCCCAC 1534
gi|34861241|ref|XM_341960.1|         CAGGATCCAT----CTGGCCTCCCACCTTGCTGA---------------- 1533
gi|16878146|gb|BC017280.1|BC01       CAGCACCAGCTGGCCGGGCCTGCCCCCTTGCTGAGCACCCCTGCTCCCGA 1692
                                     *** * *       * ***** ** *********

gi|26327464|dbj|AK031609.1|          ATCGCCCGGCTACCAGCCAAGCTCCAAGTTGTCCTGCCCCACTAAGAGGA 1584
gi|34861241|ref|XM_341960.1|         ----------------------------------------------------
gi|16878146|gb|BC017280.1|BC01       G--GCCCGGCCCGTGATCGGG---------GCCCTGGGGCTGTGAGA--- 1728

gi|26327464|dbj|AK031609.1|          GCCCCGGGGTGGAACAAGATCCTGTCTGCCCCGGCTCTCCCCCTTACATG 1634
gi|34861241|ref|XM_341960.1|         ----------------------------------------------------
gi|16878146|gb|BC017280.1|BC01       -CCCCGACCCTCTCGAGGAACC---CTGCCTGAGACGCCTCCATTAC-CA 1773

gi|26327464|dbj|AK031609.1|          CTGTGGAATGAGGACATAGGACCCTGCACAGCTGCAAGTGGGCTTTCGAT 1684
gi|34861241|ref|XM_341960.1|         ----------------------------------------------------
gi|16878146|gb|BC017280.1|BC01       CTGCGCAGTGAGATGAGGGGACTCACAGTTGCCAAGAG-GGGTCTTTGCC 1822
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gi|26327464|dbj|AK031609.1|        GTGAAACCTTTCACCAGCCACTCACTATGCTACTCCTGGTGGGGAGGGAT 1734
gi|34861241|ref|XM_341960.1|       ----------------------------------------------------
gi|16878146|gb|BC017280.1|BC01     GTGGGCCCCCTCGCCAGCCACTCACCA-GCTGCATGCACTGAGAGGGGAG 1871

gi|26327464|dbj|AK031609.1|        GGGGAGTCGCCCTCCCCCGGAGCCCACAGAGCCCTCCCCCGTCACGTC-- 1782
gi|34861241|ref|XM_341960.1|       ----------------------------------------------------
gi|16878146|gb|BC017280.1|BC01     GTTTCCACACCCCTCCCCTGGGCCGCTGAGGCCCCGCGCACCTGTGCCTT 1921

gi|26327464|dbj|AK031609.1|        ACCTGTGCCTTACTCCTGCCCACCA--CCTTTTCAGTGCAGGGTCAGTCT 1830
gi|34861241|ref|XM_341960.1|       ----------------------------------------------------
gi|16878146|gb|BC017280.1|BC01     AATCTTCCCTCCCCTGTGCTGCCCGAGCACCTCCCCCGCCCCTTTACTCC 1971

gi|26327464|dbj|AK031609.1|        TAAGAACTCCACATCTGCTGCTGC-TCCCTGGTGTCCAAGTTTCCTTGCA 1879
gi|34861241|ref|XM_341960.1|       ----------------------------------------------------
gi|16878146|gb|BC017280.1|BC01     TGAGAACTTTGCAGCTGCCCTTCCCTCCCCGTTTTTCATGGCCTGCTGAA 2021

gi|26327464|dbj|AK031609.1|        GA--GTGTGTGAAGAATTATTTATTTTTGCCAAAGCAGATCTAATAAAAG 1927
gi|34861241|ref|XM_341960.1|       ----------------------------------------------------
gi|16878146|gb|BC017280.1|BC01     ATATGTGTGTGAAGAATTATTTATTTTCGCCAAAGCACATGTAATAAATG 2071

gi|26327464|dbj|AK031609.1|        CCACAGCTCAGCTTCTGCCTTCCTCACTTCTGCATGCT------------ 1965
gi|34861241|ref|XM_341960.1|       ----------------------------------------------------
gi|16878146|gb|BC017280.1|BC01     CTGCAGCCCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA 2121

gi|26327464|dbj|AK031609.1|        -          (SEQ ID NO:12)
gi|34861241|ref|XM_341960.1|       -          (SEQ ID NO:15)
gi|16878146|gb|BC017280.1|BC01     A 2122     (SEQ ID NO:1)
```